

# South African Medical Journal

## Suid-Afrikaanse Tydskrif vir Geneeskunde

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Cape Town, 23 June 1956  
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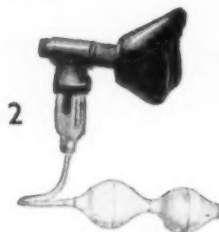
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### RHINOSCLEROMA (SCLEROMA)

#### REPORT OF A CASE IN SOUTH AFRICA

B. J. P. BECKER, M.D., D.P.H., D.T.M. & H.  
and

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Rhinoscleroma (syns.: scleroma, 'scrofulous lupus of the nostrils') is a specific chronic granuloma localized in the rhinopharyngeal tract and involving the tissues of the nose, sinuses, pharynx, larynx, trachea and bronchi. Although the disease is now stated to be world-wide,<sup>1</sup> so far as the authors are aware this is the first report of a case in South Africa.

The literature has been reviewed in 1946,<sup>1</sup> 1949,<sup>2</sup> and 1955.<sup>3</sup> The disease was first described by the Viennese dermatologist von Hebra in 1870, but it had undoubtedly existed in Eastern Europe for many years before that time.<sup>2</sup> Important milestones in the history of the condition are the description of the characteristic Mikulicz cell in 1876 and the isolation of the *Bacillus rhinoscleromatis* by von Frisch and Pellizari in 1882. In 1932 the Second International Congress of Otorhinolaryngology had collected 2,361 cases for discussion.

**Incidence.** There are now few countries in the world where cases have not been reported, but in many of them it is very uncommon in native-born inhabitants; e.g., in the USA up to 1949, 102 cases had been reported, only 13 of which were not in immigrants.<sup>2</sup> The disease appears to be particularly common in Central and Eastern Europe, Central America (El Salvador and Guatemala)<sup>1</sup> and in Indonesia.<sup>4</sup>

**Etiology:** Although the specific etiology is disputed, most authorities accept the *Klebsiella rhinoscleromatis* (Frisch bacillus) as the causative agent. This bacillus is a member of the Friedlander group and is biochemically<sup>5</sup> and immunologically<sup>6</sup> a distinct species. It can be isolated from cases with regularity and occurs as an intracellular inhabitant in the lesions. Cases of the disease exhibit positive intracutaneous skin tests to its antigens, and complement fixation and agglutination reactions have further confirmed its specificity.<sup>5</sup> More-

over, beneficial results with antibiotic treatment have been reported.<sup>7-10</sup> Levine<sup>11</sup> failed to find biochemically typical *Klebsiella* organisms in over 500 cultures from persons with or without disease of the ear, nose and throat other than rhinoscleroma. However attempts to reproduce the disease by various types of inoculation into humans has failed<sup>1</sup> although very similar histological lesions have been produced in white mice.<sup>11</sup> Thus Koch's postulates have not been fulfilled and some workers are concentrating on a possible virus etiology.<sup>1</sup> The disease occurs at all ages and in both sexes. It is most frequently seen in early adult life. Several reports of multiple cases in families have been reported. Its incidence is greatest at the poorer socio-economic levels.

**Transmission.** Transmission experiments have failed and the exact mode of infection remains unknown. Probably long exposure is necessary.<sup>3,4</sup>

**Pathology.** The condition begins slowly and insidiously, usually in the nasal septum or alae and spreads by peripheral extension to the nasopharynx, sinuses, larynx, trachea and bronchi, and less commonly to lips, tongue, uvula, soft palate, orbit, lacrymal passages, eustachian tubes and tympanic cavity. The condition is a submucosally infiltrating granuloma with pathognomonic histological features. A variety of clinical appearances are produced, e.g. atrophic rhinitis, localized nodules, polypi, and diffuse infiltrations. Untreated it pursues a chronic relentless course producing gruesome facial deformities. Bony and cartilaginous structures are not involved. Progressive fibrosis and cicatrization in the healing phase may lead to further deformities. The course may extend over a period of many years.

**Histopathology.** In very early cases there may be only massive plasma-cell infiltration with the characteristic bacilli lying free in the tissue spaces. Shortly

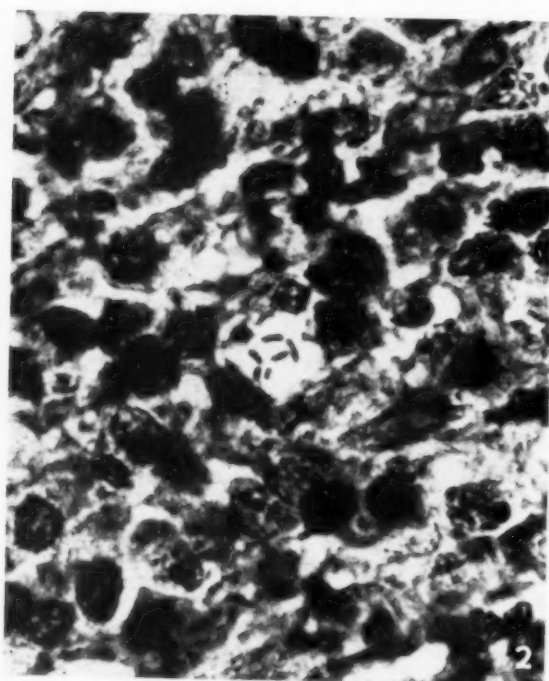
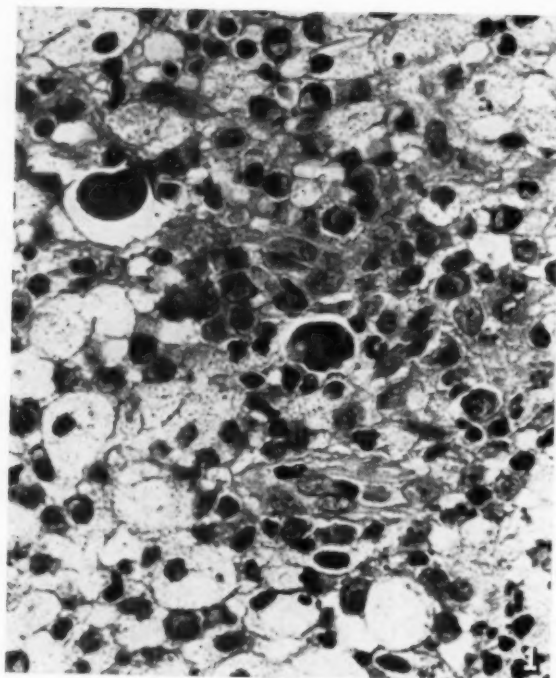


Fig. 1. Rhinoscleromatous granuloma. Stained H. and E.  $\times 600$ . The section shows sheets of typical Mikulicz cells separated by a fibrous trabecula which is infiltrated by plasma cells. Two typical Russell bodies are present in the centre of the field.

Fig. 2. Rhinoscleromatous granuloma. Warthin-Starry technique  $\times 1500$ . The section shows the typical rod-like bacilli lying within a Mikulicz cell.

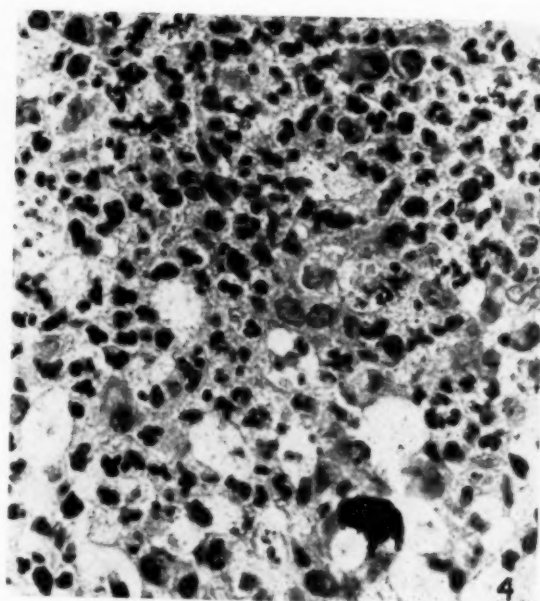
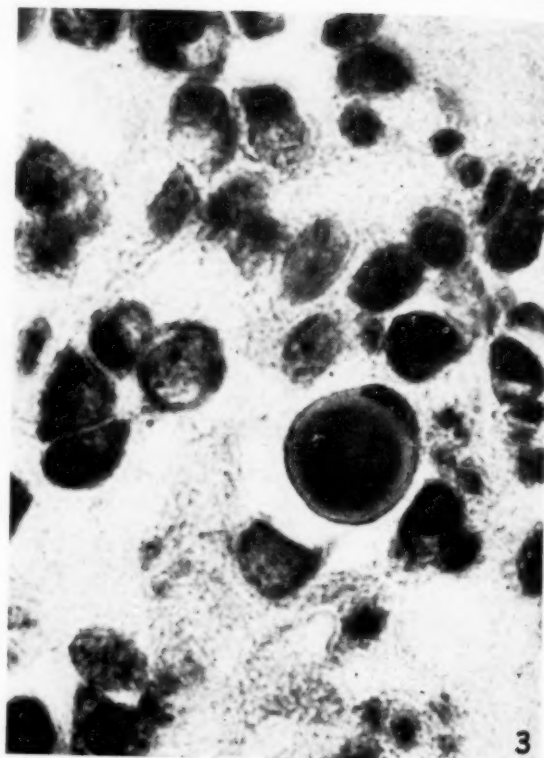


Fig. 3. Rhinoscleromatous granuloma. Giemsa stain  $\times 1500$ . The section shows a Russell body in an intracellular position.

Fig. 4. Rhinoscleromatous granuloma. Stained H. and E.  $\times 400$ . The section shows a micro-abscess.

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thereafter the Mikulicz cell appears, and in the active phase these cells are found in masses and sheets separated by fibrous trabeculae heavily infiltrated with plasma cells and a few lymphocytes (Fig. 1). The Mikulicz cell is probably a tissue histiocyte. They are large pale cells ( $50 \mu$ ) with small intensely pyknotic nucleus and foamy vacuolated cytoplasm. With the PAS stain, thin condensed cytoplasmic Schiff-positive partitions radiate out from the nucleus towards the cell boundary, but the intervening cytoplasm is unstained. Frozen sections stained with Oil Red O show no neutral fat. With bacterial stains, or with the Giemsa stain, many of the Mikulicz cells are seen to contain the characteristic rod-like bacilli (Fig. 2). These are argyrophilic and can be demonstrated in large numbers, both intracellular and extracellular, by the Warthin-Starry technique.

Russell bodies (rounded or oval hyaline masses, strongly PAS positive) are found in considerable numbers lying free and within plasma cells (Fig. 3). The fibrous trabeculae contain many dilated vessels, some of which show endarteritis obliterans. An additional feature is the presence of occasional micro-abscesses (Fig. 4). The overlying mucosa may show non-specific pseudoepitheliomatous hyperplasia. As the lesion ages, progressive vascular sclerosis and fibrosis replace the cellular elements until cicatrization is produced.

Taken as a whole, the histopathological picture in the active stage is very characteristic. Although the Mikulicz cell itself can be seen in other conditions, e.g. simple or allergic nasal polypi, and other infections of the nasal mucosa (Friedmann<sup>3</sup>), we regard the Mikulicz cell containing typical bacilli as pathognomonic.

**Clinical Picture.** As the primary site is almost always in the nose, the disease often begins with the symptoms and signs of rhinitis, with ozoena, nasal discharge and epistaxis. Sense of smell may be preserved, for the olfactory cleft is not early involved. Later, progressive painless nasal obstruction is the main complaint. Intranasal inspection may show nodules, polypi, or diffuse infiltrations. Invasion of other structures produces symptoms due largely to mechanical obstruction and loss of function: viz. *larynx*—hoarseness, coughing, aphonia; *pharynx*—dysphagia; *tongue*—difficulty in speech; *middle ear*—deafness.

No pyrexia or constitutional symptoms are produced until late, when anorexia, weight loss and cachexia appear.

**Diagnosis.** A definite diagnosis may be established by biopsy, but this should be confirmed by cultural methods. Complement—fixation reactions, and agglutination and skin reactions are not to our knowledge available as yet in South Africa.

**Prognosis.** This used to be very poor, because spontaneous cure was rare and induced cures almost as uncommon. Progressive spread of the condition led to respiratory obstruction and death from intercurrent infection. New hope now awaits sufferers with planned surgery and antibiotic treatment. The organism has been proved sensitive to streptomycin, aureomycin, terramycin and chloromycetin, and apparent cures are being reported.<sup>7-10</sup>

#### REPORT OF CASE

J.P., an Indian boy aged 13 years, was born in South Africa, but was taken to India by his family when he was 2 years old and lived in a village in Bombay from 1945 to 1947. He now lives in Boksburg North and there are no other cases in the family of 2 adults and 9 children. His main complaint was blockage of the left nostril, and symptoms of this had been present for 2 years. During the last 2 months he had suffered frequent episodes of epistaxis and excessive sneezing.

On examination of the left nostril a large haemorrhagic polyp of the inferior turbinate,  $\frac{1}{2}$  inch in diameter, was found. Similar smaller polypi were found on the posterior part of the right inferior turbinate. His general condition was excellent and no facial deformity was present. He was afebrile. The larynx was normal. The polypi were removed surgically and sent to us for histological examination.

**Histology.** The characteristic histological features of rhinoscleroma were observed (Figs. 1-4) and the diagnosis was made on histopathological grounds.

**Bacteriological examination** was made a few days after operation. In the meantime, the patient had been treated with crystalline penicillin. Swabs taken from both nostrils resulted in the isolation in pure culture of a bacillus with the characteristic morphological and biochemical features of *K. rhinoscleromatis*. The bacteriological studies were undertaken by Dr. V. Bokkenheuser of the South African Institute for Medical Research and we are indebted to him for the following detailed report:

The bacteriological features of the organism from the case (J.P.) of rhinoscleroma are as follows:

Primary culture on blood agar yielded an almost pure culture of a Gram-negative non-motile bacillus. The colonies were large and mucoid (Fig. 5) but capsules could only be demonstrated by intraperitoneal injection of the organism suspended in mucin into mice (Fig. 6).

The culture fermented the following carbohydrates with production of acid only: glucose, mannitol, saccharose, maltose, salicin, adenite, xylose, sorbitol (after 6 days in-

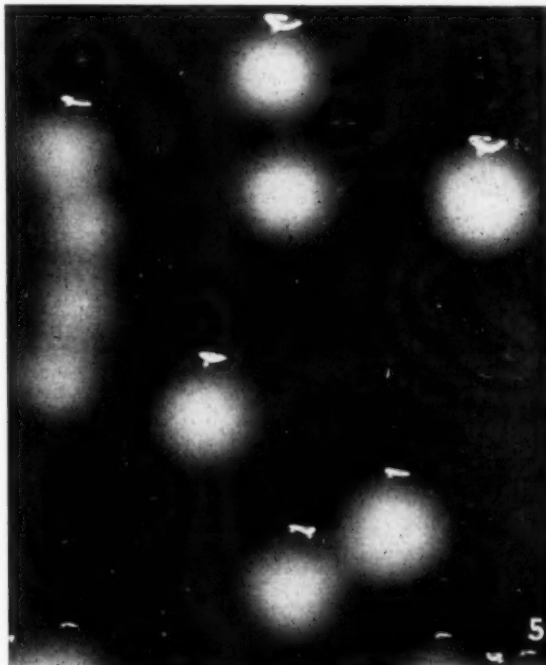


Fig. 5. *Klebsiella rhinoscleromatis*. The plate shows the mucoid colonies on blood agar.

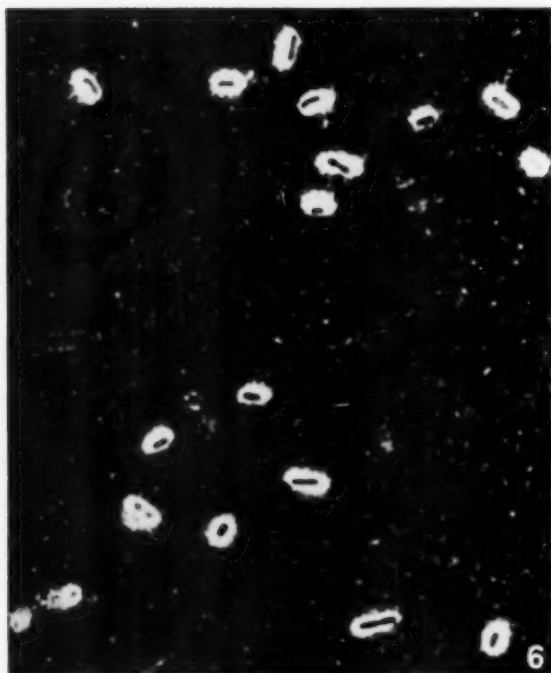


Fig. 6. *Klebsiella rhinoscleromatis*. Indian-ink preparation. The plate shows the encapsulated organisms.

cubation at 37°C), rhamnose, laevulose, dextrin, arabinose, glycogen and glycerol (after 10 days of incubation). Lactose and dulcitol were not fermented. The H<sub>2</sub>S, indol, urea citrate and Voges-Proskauer tests were negative.

Gelatin was not digested. The methyl red and nitrate tests were positive.

The organism has thus all the characteristics of the *Klebsiella* organisms described in cases of rhinoscleroma (Kauffmann<sup>14</sup>).

A culture of the organism was sent to the Statens Serum Institut, Copenhagen, for typing of the capsular antigen. Dr. Ida Orskov reported as follows: 'Biochemically the strain is designated as *Klebs. rhinoscleromatis*, and serologically it belongs to capsule type 3.'

Sensitivity tests showed the following spectrum of sensitivity: penicillin negative, streptomycin 2, sulphathiazole negative, aureomycin 2, chloromycetin 2, terramycin 2, erythromycin 3, achromycin negative.

In view of this bacteriological report, further treatment with streptomycin and erythromycin has been advised.

#### DISCUSSION

The diagnosis of rhinoscleroma in this case has been established beyond doubt. From the history it appears that it must be regarded as an imported case; infection probably took place in India during the child's residence there in 1945-47. It is well known that the condition is prevalent in India and hitherto has been unknown in South Africa. The incubation period and evolution of the disease extended over a period of 7-9 years before the first symptoms were produced. A further 2 years elapsed before treatment was sought—a good illustration of the slow progress and chronicity of the disease. Further extensive antibiotic treatment to sterilize the site of infection is now urgently indicated.

#### SUMMARY

1. The first case in South Africa of rhinoscleroma is reported.
2. A brief review of the literature of the condition is presented.
3. Diagnosis in well established cases can be confidently made on histological grounds.

We wish to thank Dr. V. Bokkenheuser of the South African Institute for Medical Research for his expert assistance in the bacteriology, Dr. Ida Orskov of the Statens Serum Institut, Copenhagen, for typing the capsular antigen, Dr. T. Pienaar for his clinical assistance, Mr. M. Ulrich for the photography, and Mr. D. Lloyd for his unstinted technical assistance.

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#### UNION DEPARTMENT OF HEALTH BULLETIN

Union Department of Health Bulletin. Report for the 8 days ended 7 June 1956.

Plague. Nil.

Smallpox, Cape Province. One (1) Coloured case in the Kenhardt district.

Typhus Fever, Cape Province. One (1) Native case in the Mount Frere district. Diagnosis confirmed by laboratory tests.

No further cases have been reported from the Cradock district since the notification of 9 May 1956. This area may now be regarded as free from infection.

Epidemic Diseases in Other Countries.

Plague: Nil.

Cholera in Calcutta (India); Chalna, Chittagong, Dacca (Pakistan).

Smallpox in Rangoon (Burma); Ahmedabad, Allahabad, Bombay, Calcutta, Delhi, Jodhpur, Madras, Visakhapatnam (India); Dacca (Pakistan); Mombasa (Kenya); Tanga (Tanganyika).

Typhus Fever in Cairo (Egypt).

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# South African Medical Journal

## Suid-Afrikaanse Tydskrif vir Geneeskunde

### VAN DIE REDAKSIE

#### WAT NIE DOOD MAAK NIE

„Wat kan ek eet, Dokter?” Hoe dikwels het ons nie al daardie woorde gehoor nie, en hoe dikwels het ons nie al skynbaar geleerde raad gegee nie! Het ons al ooit 'n halwe vermoede gehad dat baie van ons raadgewings op niks grondiger as tradisie berus nie, en dat die tradisie ons al soms in die steek gelaat het? Hoewel die tradisie dikwels reg het, moet ons tog die feite wat ons dusver as onbetwisbaar aanvaar het, krities en met 'n bietjie meer wetenskaplike noukeurigheid ondersoek. Ons behoort te vra watter bewys daar is dat die voedsel wat 'n pasiënt meen dat hy kan geniet, hom inderdaad kan kwaad doen.

Daar is baie voor die hand liggende voorbeelde; laat ons 'n paar bespreek. Ons dink dadelik aan vetsug, wat byna altyd aan ooreet te wyte is. As vetsug die gesondheid benadeel—volgens die lewensversekeringskaarte is dit blykbaar die geval—dan kan dieetbeperking wel nodig wees. Suikersiekte is nog 'n uitstaande voorbeeld. Sommige skrywers raai wel aan dat suikersiektelers 'n onbeperkte voedselkeuse toegelaat moet word, maar ten minste een van hulle het intussen sy woorde teruggetrek en teruggekeer na die streng beheer van die pasiënt se dieet.<sup>1</sup> Hoewel die feite nog 'n beslissing afwag, kan kroonslagaarsiekte en die vetgehalte van die dieet ook aangehaal word.

Jare lank is pasiënte met maag- en dundermsere met 'n streng beheerde voedselplan behandel. Baie van die ouer geneeshere sal die strafheid van die skrale dieet onthou. Die honger pasiënte het om kos gesmeek, maar dit is hulle streng verbied. Wat voedsel betref, was die saak maar haglik vir dié met bloeiende maag- en dundermsere—al wat hulle mondeliks kon neem, was ys om aan te suig. Die sterftesyfer was hoog. Toe het Meulengracht bewys dat beter resultate behaal kon word as die pasiënte 'n feitlik onbeperkte dieet toegelaat word. Die teenstrydigheid dat die pasiënt met die bloeiende maagseer groot en voedsame maaltye kon geniet terwyl die nie-bloeiendes liggaam en siel op brood en pap kos aanmekeer moes hou, was darem te ooglopend, en binnekort het die diëte meer toegewend geword. Die meeste geneeshere het nietemin daarop aangedring dat die voedsel ten minste sag en glad moet bly. Nou lyk dit asof selfs hierdie bepaling nie essensieel is nie. Dit is bewys<sup>2,3</sup> dat pasiënte wat die gewone hospitaaldiëet mag hou, met inbegrip van rowwigheid—selfs ook vark-

### EDITORIAL

#### A LITTLE OF WHAT YOU FANCY

„What may I eat, Doctor?” How often have we heard those words, and how often have we given apparently erudite advice! Have we ever had a lurking suspicion that much of what we are saying is based on nothing sounder than tradition, which has sometimes let us down? While tradition is often correct, it still behoves us to examine critically and with a little more scientific precision what we have hitherto accepted as unquestionable. We should ask what evidence there is that a food which a patient feels he can enjoy is in fact bad for him.

Many examples spring to mind; let us consider a few of them. Obesity is perhaps the most obvious one. It is almost invariably due to overeating. If obesity is harmful—and the life-insurance tables seem to show that it is—then dietary restrictions may be necessary. Diabetes is also a conspicuous example. Unrestricted choice of food has been advocated for diabetes by some authors but at least one of these has since recanted and gone back to a strict control of the patient's diet.<sup>1</sup> Coronary-artery disease and the fat content of the diet may also be quoted, though the facts are still *sub judice*.

For many years patients with gastric and duodenal ulcers were treated with a strict dietary regime. Many older doctors will recall the rigours of the sippy diet. Hungry patients clamoured for food, which was sternly denied them. For patients bleeding from these ulcers the outlook, dietetically speaking, was frightful—nothing by mouth except ice to suck. The mortality rate was considerable. It was then shown by Meulengracht that better results could be obtained if the patients were allowed what amounted almost to an unrestricted diet. The paradox that the patient whose ulcer was bleeding was allowed to eat large and substantial meals while the non-bleeding ulcer patient had to subsist on bread and slops was too obvious to be missed, and more liberal diets soon followed; but most doctors insisted, at least, that the bland and soft nature of the diet should be maintained. Now it appears as though even this is not essential. It has been shown<sup>2,3</sup> that patients who are allowed to have the usual ward diet, not excluding roughage—or even pork-pie—fared slightly better than those fed with the traditional 'bland'

pastei—ietwat beter gevaar het as dié wat die gebruiklike sagte kos gekry het. Daarvan is die verbasende afleiding gemaak dat die gebruiklike dieetkundige behandeling wat vandag vir maagseer toegepas word, nie die genesing van die seer bevorder nie, maar dit selfs kan vertraag. Pasiënte wat medies reeds goed ingeprent was met die idee van die 'regte' dieet vir maagseerlyers, was 'n bietjie skrikkerig vir of selfs gekant teen die nuwe raad, maar toe hulle eers oortuig was, het genesing dikwels vinnig gevorder. Hulle kon die groter en meer bevredigende maaltje goed verdra en het klaarblyklik baat gevind daarby. Is streng dieetbeperkings dan nie nodig nie? Is dit nie miskien beter om die pasiënt voor te lig aangaande kossoorte wat miskien goed, of sleg, vir hom mag wees nie, en hom dan maar self te laat uitvind watter uitwerking hierdie kossoorte op sy simptome het nie? Elke ondervindingryke dokter het al pasiënte raakgeloop wie se maagseer genees het niteenstaande die feit dat hulle geheel en al geen dieetbeperkings gehou het nie. Niemand sal 'n pasiënt aanraai om iets wat sy maag omkrap te eet nie; ons bedoel slegs dat die pasiënt soms beter as die dokter weet wat hy kan verdra.

Besmetlike lewerontsteking is 'n gelyksoortige saak. Elke mediese student 'weet' dat vet hierdie pasiënte kwaad doen. Sodra 'n pasiënt met hierdie opskrif op sy bedkaart in die hospitaal opgeneem word, word hy outomaties op 'n vet-arm dieet geplaas. Baie van hierdie pasiënte kan inderdaad geen vet verdra nie. Die kwaai mislikheid maak selfs die blote gedagte aan vet afstootlik. Maar beteken dit dat vet nadelig is? Ons kry nie almal die geleentheid om hierdie saak op groot skaal uit te toets nie. So 'n geleentheid is egter onlangs gebruik, en 'n uitgebreide studie is daaroor gepubliseer.<sup>1</sup> Dit is bewys dat die beste dieet vir pasiënte met akute besmetlike lewerontsteking *nie minder* as ongeveer 3,000 kalorieë moet oplewer nie, en *nie minder* as ongeveer 150 gram elk proteïene en vet moet bevat nie. Bó hierdie hoeveelheid moet die inname *ad lib.* wees. Hoewel gebakte en vette kos spysverteringmoeilikhede kan veroorsaak, is die vette in vleis, eiers en suiwelprodukte nie nadelig by lewerontsteking nie, en dit dra immers baie by tot die smaaklikheid van die dieet. 'n Oormaat *proteïene* in die dieet kan nadelig wees vir 'n uiters siek pasiënt met 'n uitbarstende, heftige siekte of dreigende hepatiese koma, maar blykbaar ook net in hierdie soort geval. In die meeste gevalle sou dit waar wees om te sê dat die enigste belangrike ding is dat die pasiënt aanhou eet. Wat hy eet is van betreklik min belang. As hy wel vet kan verdra, is daar blykbaar geen rede waarom hy dit nie mag kry nie.

Kragtens hulle bevoorregte posisie is geneesheren in staat om die vryheid van hul pasiënte te beperk. Dit is belangrik dat die geneesheer se voorligting aangaande sy pasiënt se dieet net so modern en op hoogte van sake soos die res van sy praktyk moet wees. Op gebied van die dieetkunde is die dokter miskien gerade om 'n bietjie meer aandag aan sy pasiënt se smaak te bestee wanneer dit teenstrydig is met sy eie oorwegings.

diet. The surprising conclusion was reached that the dietetic treatment of peptic ulcer as at present practised does not hasten the healing of the ulcer and may even delay it. Some reluctance to follow the new advice, and even resistance, was met with in patients who had been medically indoctrinated with the 'correct' diet for ulcer patients, but once this had been overcome healing often proceeded apace. The larger and more satisfying meals were well tolerated and seemed to be beneficial. Are severe dietary restrictions then not required? Is it perhaps not better to indicate to the patient which foods might be helpful and which might be harmful and let him find out for himself what effect these foods have on his symptoms? Every doctor of experience has seen patients whose ulcers have healed despite the complete absence of dietary restriction. It is the rule rather than the exception. No one would advocate that a person should eat anything that upsets his stomach; what we mean to say is that the patient is sometimes a better judge of what he can tolerate than his doctor is.

A somewhat analogous state of affairs exists in infectious hepatitis. Every medical student 'knows' that fat is bad for patients suffering from this disease. No sooner does a patient come into hospital with this label on his bed-letter than he is automatically placed on a low-fat regime. Many of the patients are, in fact, intolerant of fat. The extreme nausea which goes with this disease makes even the thought of fat abhorrent. But does this indicate that fat is harmful? Opportunities for testing this out on a large scale are not available to all of us, but such an opportunity has recently been grasped and an extensive study published.<sup>1</sup> It has been shown that the optimum diet for patients with acute infectious hepatitis is one producing *not less* than about 3,000 calories and containing *not less* than about 150 grams each of protein and fat. Intake above this level should be *ad lib.* Although fried and greasy foods may cause indigestion, the fat contained in meat, eggs and dairy products is not harmful in hepatitis and adds greatly to the palatability of the diet. An excessive amount of dietary *protein* may be harmful in critically ill patients with fulminating disease or impending hepatic coma, but apparently only in this type of case. In most cases it would be true to say that the only important thing is that the patient should continue to eat. What he eats is of relatively little importance. If he can tolerate fat there appears to be every reason to give it to him.

By virtue of their privileged position doctors are able to interfere with their patients' liberty of action. It is important that the advice they offer concerning their patients' diet shall be as modern and up to date as the rest of their practice. In the field of dietetics the doctor may perhaps be wise to pay a little more attention to the patient's likes and dislikes when these conflict with the doctor's own beliefs.

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1. Dunlop, D. M. (1954): Brit. Med. J., 2, 383.

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## THE SOUTH AFRICAN POLIOMYELITIS VACCINE

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The public health measures usually adopted for preventing the spread of infection, including the isolation of cases and family contacts, the closing of nursery schools, and the prohibition of the attendance of children at places of entertainment and other public gatherings, have been singularly ineffective in preventing the spread of poliomyelitis. This is not surprising. Indeed it could be anticipated in an infection where, for every case of paralysis, there are a larger number of non-paralytic and silent cases. Both the latter forms of infection are usually unrecognized and both are capable of spreading the disease.

It was suggested<sup>1</sup> some time ago that there are two possible and likely solutions to the problem. One was the mass administration of a drug or antibiotic to eradicate poliovirus from infected individuals in a community. The other was prophylactic vaccination. It has been shown that mass chemoprophylaxis is successful in controlling epidemics of meningococcal meningitis and in eliminating the infection from closed communities, such as military camps. If a drug as effective against the virus of poliomyelitis as are the 'sulpha' drugs against meningococci were available, its mass administration to affected communities would be one method of bringing outbreaks of poliomyelitis under control. A search is being made to find such a drug and there are some promising leads. However, even if it is eventually found, it would not be the best answer to the problem, chiefly because its effect is temporary. There is more reason to put our trust in prophylactic vaccination.

Vaccination has been eminently successful in preventing two virus diseases of man, smallpox and yellow fever. There is now some reason to hope that in time it will be equally successful in preventing poliomyelitis. Broadly speaking, virus vaccines are of two kinds. Firstly, there are those consisting of living, relatively non-virulent strains of virus, such as vaccinia virus used to protect against smallpox and the 17D strain of yellow-fever virus used to protect against yellow fever. Secondly, there are the vaccines prepared from virus suspensions which have been inactivated in some way. Live-virus vaccines are generally effective, but have not always proved free from danger. Inactivated-virus or killed-virus vaccines are generally safe, but as a general rule are not as effective as live vaccines. Indeed, it has been and is still maintained by some that killed vaccines are not effective. The same objection was raised about rickettsial vaccines. We now know that provided they contain sufficient antigen, killed rickettsial vaccines will stimulate the production of antibody and at least a certain degree of protection. The difficulty, which was solved early in World War II, was to obtain sufficiently rich suspensions of rickettsiae. The same difficulty arose in attempts to prepare inactivated poliomyelitis

vaccine. It was known that the inoculation of formalized suspensions of virus, prepared from the central nervous system of monkeys and mice, stimulated the formation of antibodies in experimental animals. The difficulty was to prepare large amounts of suspension sufficiently rich in virus to produce vaccine on a large scale. This difficulty was solved in 1949, when Weller, Enders and Robbins<sup>2</sup> found that poliovirus would grow in tissue cultures of human cells. This discovery led to the tremendous advances that have been made in our knowledge of poliomyelitis within the last 5 years. In 1952 we had the privilege of listening to a lecture by Dr. Weller on the application of the tissue culture in the study of virus diseases. It was clear that this technique could be applied to producing large amounts of virus suspension such as are needed for the preparation of inactivated vaccines. The technique could also be applied to the development of non-virulent strains of virus for use as living poliomyelitis vaccine, in the same way as the 17D strain of yellow-fever virus was evolved. Attempts are being made in several laboratories, including our own, to develop such strains, and already some success has been achieved in this endeavour. The situation has recently been reviewed by Koprowski<sup>3</sup> and by Sabin.<sup>4</sup> Many feel that this type of vaccine will provide a better answer to the problem of immunization than an inactivated vaccine. However, at present we are concerned with the latter type.

Dr. Jonas Salk, aided by the National Foundation for Infantile Paralysis in the United States of America, undertook the task of developing such a vaccine. He and his colleagues of the University of Pittsburgh in a long series of studies<sup>5</sup> have worked out methods of producing rich suspensions of poliovirus and have defined conditions for the inactivation of the virus suspensions with formaldehyde. A similar task was undertaken by a team under Dr. P. D. Winter in the Laboratories of the Poliomyelitis Research Foundation.

Since the pioneer work of Sir Spencer Lister, which led to the large-scale production of pneumonia vaccine, the South African Institute for Medical Research has been responsible for the production of a number of vaccines and has amassed a considerable experience of the processes involved. Several of those engaged in the study of the problems of producing poliomyelitis vaccine had previously been associated during World War II and subsequently with the production of yellow-fever vaccine and formalized vaccines against typhus fever and influenza, and more recently with the study of vaccination against Newcastle disease and Rift Valley fever. This previous experience served as a guide in solving some of the problems which arose in the production of poliomyelitis vaccine. In the early stages of the work we had the benefit of a visit of several weeks

from Dr. T. H. Weller who, as already mentioned, was responsible with Professor Enders and Dr. Robbins for the crucial discovery that poliovirus would proliferate in tissue cultures of human cells. He initiated the team at the South African Institute for Medical Research in the technique and procedures of tissue culture. In the later stages we were in regular correspondence with those in the United States, Canada, Britain and Sweden engaged on similar or related projects, in particular with Dr. Weller, Dr. Jonas Salk, Dr. Albert Sabin, Dr. Workman, Dr. Murray and Dr. Sven Gard, to all of whom we are greatly indebted for keeping us informed of the latest developments in the United States. Many of their techniques and procedures were adopted in the manufacture of the South African vaccine, which in general but with some modifications followed the principles and practice described fully by Dr. Salk.<sup>5</sup>

#### ACCOMMODATION

It may be recalled that in 1948, after an extensive epidemic of poliomyelitis, a National Committee under the chairmanship of Mrs. E. Gordon, then Mayoress of Johannesburg, launched an appeal for funds to support research into poliomyelitis. The response of the public of Southern Africa was very generous and over £500,000 was collected. A Board of Trustees, with Mr. H. W. Anderson as Chairman, was appointed to administer this fund. The objects of the Poliomyelitis Research Foundation, which thus came into being, have been set forth in the constitution. These briefly are, firstly, to carry out research into poliomyelitis, virus diseases generally and related problems and, secondly, to provide a vaccine against poliomyelitis.

To further these objects the Laboratories of the Poliomyelitis Research Foundation were built by agreement with the Union Government in the grounds of the South African Institute for Medical Research at Rietfontein. But for the generous support of the Appeal, large-scale production of poliomyelitis vaccine in South Africa could not have been undertaken. Although at the time there appeared to be no immediate prospect of large-scale production of poliomyelitis vaccine, provision for this work was made in the original plan. A whole wing of the institution was planned and is now set aside solely for the production and testing of vaccine. This has been equipped with all the apparatus necessary for this purpose. Separation of accommodation, apparatus and glassware is rigidly enforced to guard against cross-contamination with other infectious agents. Change rooms are provided at the entrance, where the staff change from their outdoor clothes into a working uniform, and before handling tissue cultures are gowned and gloved as for an aseptic surgical operation. The preparation of tissue cultures and their inoculation and harvesting is carried out under hoods equipped with ultra-violet light, and all air coming into the laboratories is filtered to ensure sterility.

#### METHOD OF PRODUCTION

##### *Preliminary Studies*

The first problem was to devise a method for the regular production of rich suspensions of poliovirus.

As previously it had been found that formalin-inactivated rickettsial and Rift-Valley-fever virus vaccines were not effective in stimulating antibodies unless they were prepared from suspensions with a titre of at least  $10^{-4}$ , it was decided that the aim in the case of poliovirus should be suspensions of a minimum titre of  $10^{-6}$  virus particles per ml. Early studies showed that the yield from cultures of monkey testicular cells rarely exceeded  $10^{-5}$ . The various tissue-cells of the common vervet monkey were then tested to determine which gave the best yields. It was found that tissue cultures of kidney and lung gave the richest growths of virus. Lung cultures, not unexpectedly, were often contaminated by fungi. Kidney-cell preparations were thus preferred. At first suspended-cell tissue-cultures were used, but cultures of trypsin-dispersed kidney-cells prepared according to the method described by Younger<sup>6</sup> have been used for the past 2 years.

Formalin was chosen as the inactivating agent because it has been used for this purpose in the past in the rickettsial and other virus-vaccines prepared at this Institute. Studies of the concentration required for inactivation were undertaken, but the results of the detailed investigations of Dr. Salk on the inactivation of poliovirus with formalin at different concentrations and at different temperatures became available. He defined accurately the conditions under which inactivation occurs and recommended a concentration of 1:4000 formalin acting at a temperature of 37°C for a period 3 times longer than was required to eliminate demonstrable active virus. The exact time is defined by determining the rate of inactivation shown by titrating samples of the virus suspension taken at regular intervals and plotting the line of inactivation. It was found that this was usually complete in about 72 hours. Our method of inactivation was based on his findings. However, it became apparent that the process of inactivation was somewhat uncertain under these conditions. To meet the difficulty it was decided to ensure that adequate formalin was present throughout the process of formalinization by adding another amount of 1:4000 formalin to the suspension on the 9th or 10th day and allowing it to act until the 12th day after the start of the process. The formalinized suspension was then placed in a 4°C refrigerator, where it remained until the results of the various tests became available. These revealed that the potency in stimulating antibodies was not adversely affected in experimental animals.

The value of additional treatment with ultra-violet light to ensure safety has been investigated, with promising results, which will be reported separately.

The value of B propio-lactone as an inactivating agent has also been studied and it has been found to be most effective without at the same time destroying the antigenicity. While this substance may have an important part to play in their preparation in the future, the vaccine to be issued this year has not been exposed to it.

##### *Strains of Virus*

The origin of the strains of the virus used originally in the preparation of the virus was as follows:

Type 1, Brunhilde strain, sent to us by Dr. Thomas H. Weller from Professor Enders' laboratory in the Children's Medical Centre of Harvard University, Boston, United States of America.

Type 2, Collans strain, isolated by Professor van den Ende in Cape Town from the central nervous system of a fatal case in an adult.

Type 3, Templeon strain, isolated by Dr. H. H. Malherbe of these Laboratories from faeces of a child—one of a number of children found to have silent infections, who had been in contact in a nursery school with a child who died of bulbar poliomyelitis.

These strains were chosen because it was found that they regularly gave prolific growths of virus in tissue culture. The representatives of Type 2 and Type 3 were locally isolated. Our local representative of the Type-1 strain at that time appeared to be more than usually virulent in monkeys and for that reason the Brunhilde strain was preferred over it and over the Mahoney strain, which was also considered and which was included in the vaccine produced in the United States.

These strains of virus are all virulent and, after the accidents in the United States, it was decided to substitute less virulent strains for them. These less virulent strains were obtained from Dr. Albert Sabin, who has made a special study of their pathogenicity.<sup>4</sup>

At present the strains used are the following:

**Brunenders strain:** A variant of the Brunhilde virus obtained by Professor Enders after 20 passages of the Brunhilde virus in tissue culture. This strain is much less virulent than its parent in that it no longer regularly produces paralysis in monkeys. However, after intracerebral and intraspinal inoculation of monkeys, it still produces lesions in the central nervous system. It was then inoculated into chimpanzees by Dr. Sabin. The virus obtained from the faeces of one of these chimpanzees was then passed 4 times in cynomolgus kidney cell cultures. After being received in our laboratories it was passed 3 times in *Cercopithecus* monkey kidney cell cultures. The third harvest, a large one, is stored in ampoules in a CO<sub>2</sub> box and is used as seed for the inoculation of the tissue cultures for the preparation of Type-1 poliovirus suspensions.

**Fallans strain,** the representative of Type-2 poliovirus in the later batches of vaccine, was isolated by Dr. Sabin from the rectal swab of a healthy child. It has been passed in cynomolgus kidney cell cultures, including the rapid transfer of large inocula, followed by 3 passages at limiting dilution to separate non-virulent from virulent virus-particles. We received a sample of the 27th kidney passage labelled Cincinnati FAF 117, kidney passage 27 of 26.3.55. After being passed 3 times in our laboratory, the harvest of the third passage has been stored in ampoules in the CO<sub>2</sub> box and is used as seed for the inoculation of tissue cultures in the preparation of suspensions of Type-2 poliovirus.

**Leonav strain,** the representative of Type-3 poliovirus, was also obtained from Dr. Sabin, and is a relatively non-virulent variant of the parent Leon strain separated out by his limiting dilution technique. The sample sent has been passed 35 times in cynomolgus monkey kidney tissue culture. It has also been passed 3 times in our laboratory in *Cercopithecus* monkey-kidney tissue cultures. The third harvest was ampouled and is also stored in the CO<sub>2</sub> box to be used as seed in the preparation of suspensions of Type-3 poliovirus.

These 3 strains are not entirely non-virulent. Monkeys inoculated with high dilutions of them intracerebrally and intraspinally develop no signs of illness or paralysis and show few, if any, lesions apart from those caused by trauma in the spinal cord. Monkeys inoculated in this way with more concentrated suspensions of virus may occasionally develop weakness or actual paralysis, but sections of their spinal cord often show lesions of poliomyelitis.

### Monkey Supply

To prepare vaccine on a large scale it was necessary to arrange for an adequate supply of vervet monkeys, *Cercopithecus aethiops pygerythrus*, which had been shown to be eminently suitable for this work. Although these monkeys are numerous in South Africa, this has not always been easy. The principal supply has come from the Northern Transvaal and was arranged by the late Dr. Annecke, Deputy Chief Health Officer of the Union Health Department. We are especially indebted to Mr. Combrinck of his staff, whose untiring efforts over a long time kept us supplied with adequate numbers when otherwise there would have been a serious shortage. A supply arranged by Dr. Ferguson, Chief Regional Health Officer for Natal, was also received from the environs of Durban and Zululand. Another large supply, arranged by Dr. Harington and Mr. Clegg of the Port Elizabeth Branch of the South African Institute for Medical Research, has come from the Eastern Province. More recently, monkeys have come from many of the districts of South Africa where they abound. We are grateful to all those concerned for their contributions, without which of course it would not have been possible to produce poliomyelitis vaccine.

The monkeys were transported to the Laboratories by rail, and the officials of the South African Railways arranged for their speedy delivery. After arrival they were kept for a variable time on a good diet to improve their condition and to test their tuberculin reactions. Incidentally, it is of interest to note that, with one exception, these proved negative.

### PREPARATION OF VACCINE

After the completion of these preliminary studies and arrangements, the routine procedures adopted by Dr. Winter and his team in the preparation of poliomyelitis vaccine are briefly as follows:

#### 1. Preparation of kidney cell cultures

The kidneys are removed from the monkeys under anaesthesia in an operating theatre supplied with filtered air, and collected in sterile containers. In the tissue-culture laboratory, after removal of the capsule, pelvis and calyces, the kidneys are cut into small pieces. The tissue is then treated with trypsin to disperse the epithelial cells. 0.25% trypsin in Dulbecco phosphate buffer is added and allowed to act for 10 minutes in an Erlenmeyer flask and stirred with a magnetic stirrer. It is then allowed to sediment. The first supernatant is discarded. This procedure is repeated 8–10 times, but the second and later supernatants are kept, and then centrifuged to throw down the cells, which are then washed 3 times by spinning down and re-suspending in phosphate buffer. After the third washing and centrifugation, the cells are re-suspended to a concentration of 500,000 cells per ml. in the growth medium consisting of a 0.5% solution of lactalbumen hydrolysate in Hanks balanced salt solution to which 5% bovine serum is added. This cell suspension is then distributed into Blake flasks or Roux bottles in 150 ml. amounts. The bottles are tightly corked with rubber stoppers and incubated lying flat in a 37°C incubator-room for

5-7 days. By this time the cell growth will have covered the surface of the bottle. They are now ready for the inoculation of virus, but before inoculation the growth-phase medium is withdrawn and 100 ml. of the 'virus phase' or Connaught 199 medium is substituted.

## 2. Virus inoculation and harvest

The bottles are then inoculated with virus. Each bottle is inoculated with a suspension of the seed virus of a titre of  $10^{-6}$ . Destruction of the cell culture occurs in 2-3 days. When this is complete the virus suspension is harvested. The harvest in any one week consists of one type of poliovirus and, during the month, suspensions of each of the 3 types of poliovirus are prepared. These 3 suspensions are treated separately as monovalent type lots.

## 3. Titration and confirmation of identity of virus

The suspension is first filtered through a coarse Seitz filter-pad and then through 2 ultra-fine frittered glass filters in series. Samples of the filtered suspension are taken to determine the titre of the virus. This is done by preparing serial tenfold dilutions and inoculating each in 0.1 c.c. amounts into 3 tissue-culture tubes, which are then incubated at  $37^{\circ}$  in a roller drum. The reading of the tubes is taken on the 3rd day after inoculation.

The identity of the virus in the suspension is confirmed by putting up neutralization tests with specific antisera against the 3 types of poliovirus in roller tubes, and confirming that it is neutralized by the corresponding antiserum.

## 4. Formalinization

Filtered air is then bubbled through the suspension overnight, the pH is then adjusted to pH 7 with 0.1 N hydrochloric acid and, within 72 hours of the primary filtration, formalin is added.

The B.P. solution of formaldehyde is tested to confirm that it is of standard strength; then a dilution of 1:100 is prepared and this is then added slowly with frequent stirring in sufficient amount to the virus suspension to give a final dilution of 1:4000 formalin. The formalinized suspension is then incubated in a water-bath at  $37^{\circ}\text{C}$  for 5-7 days. It is then again filtered through 2 ultra-fine frittered glass candles in series, and then is irradiated with ultra-violet light in a dose sufficient to destroy virus of a concentration of  $10^{-3}$  per ml.

## 5. Control of inactivation

Samples of the suspension are taken at regular intervals from the 1st to the 3rd day of inactivation and these are titrated in roller-tube cultures to determine the presence of active virus. From the results of these tests the line of inactivation is plotted and the time taken for completion of the process is computed. The time of inactivation is continued for 3 times that indicated by this diagram. This is generally about 9 days, and on this day the first sample to be tested for active virus, according to the requirements of the safety tests, is taken.

The formalinization process is then continued for another 3 days, when the second sample is taken. These 2

samples are tested according to the standards laid down in the safety-test regulations for active virus. These tests take several weeks, and during this time the suspension is stored in a refrigerator at  $4^{\circ}\text{C}$ . During this time also the suspension is tested for potency, i.e. its ability to stimulate the formation of antibody in inoculated guinea-pigs, monkeys or both.

Cultures are made on bacteriological and mycological media to exclude bacterial and fungal contaminants.

## 6. Preparation of pool

Provided that the monovalent suspensions are found to be free of active virus and potent, a pool is prepared by mixing 3 lots representative of the 3 types of poliovirus and each of about 30 litres volume and the pool is thoroughly mixed. These pools are then submitted to the prescribed safety and potency tests. If the results are satisfactory, the pool is ampouled and bottled. The final containers are then tested again as prescribed in the safety regulations.

## POTENCY TESTS

The potency of the vaccine was determined by antigenicity tests on animals. Most laboratories in the United States have used monkeys for these tests. However, the antibody response of monkeys was found to be variable, even with vaccines of known good antigenicity. The use of guinea-pigs has yielded more consistent results but even with these animals a marked seasonal variation in the response has been observed by Dr. von Magnus in Denmark and Dr. Gard in Sweden. In the tests carried out in the past at the Poliomyelitis Research Foundation baboons, monkeys, and guinea-pigs have been used. Baboons and monkeys have been given, at weekly intervals, 3 intramuscular injections of 1 c.c. each and are bled before the first and 14 days after the last injection. In the guinea-pig test 5 guinea-pigs were inoculated intradermally each with 0.2 c.c. of the vaccine fluid under test. This injection was repeated after an interval of 14 days and the guinea-pigs were bled before the first inoculation and one or two weeks after the last inoculation. The pre- and post-inoculation sera from these animals were then tested in a tissue-culture neutralization test for the presence of neutralizing antibodies. In this test the serum was diluted 1 in 5 and to this dilution an equal amount of virus suspension containing approximately 100 minimal tissue-culture doses of virus was added. Three separate mixtures of serum and virus were

TABLE I. POTENCY TEST—BATCH 8

Guinea-pig No.	Before inoculation			After inoculation		
	T1	T2	T3	T1	T2	T3
1	..	..	—	+	+	+
2	..	..	—	+	+	+
3	..	..	—	+	+	+
4	..	..	—	+	+	+

+ = Protection. — = No Protection.

This neutralization test was done with  $\pm 100 \text{ TCD}_{50}$  against a final dilution of 1:10 of serum.

made, respectively consisting of serum plus Type 1, serum plus Type 2, and serum plus Type 3. These

mixtures are well shaken and allowed to stand at room temperature for 2 hours. Each mixture is then added to two or three tissue-culture tubes of trypsinized monkey kidney cells. The tubes are read on the 1st, 4th, and 7th day to detect the cytopathogenic effect of poliovirus. For a vaccine to be considered adequately potent the test must show that 75% of the animals have developed antibodies as a result of vaccination. The result of the test on Batch-8 vaccine, which was issued last year, is given in Table I.

The test at present in routine use at the Laboratories of the Poliomyelitis Research Foundation is that described by Gard and his associates in the State Bacteriological Laboratory, Stockholm. In this test, serial tenfold dilutions of the vaccine are inoculated intradermally in 0.2 ml. amounts into groups 5 guinea-pigs weighing approximately 250 g. Two weeks later, a booster inoculation of the same amount of the same dilution is administered by the same route. The animals are bled 7 days after the booster inoculation. Neutralization tests against 100 tissue-culture ID<sub>50</sub> doses of virus are set up with each serum undiluted after inactivation at 56°C. Two tissue culture tubes are seeded from each serum-virus mixture. In each test, virus and normal-serum controls are also set up. Readings are taken on the 6th day, recording which tubes show degeneration and which show none. On this basis the immunogenic extinction limit is calculated according to the method of Reed and Muench.

This test has some technical disadvantages and indeed the potency test is still being studied both here and elsewhere to evolve a standard procedure which will meet with general approval.

#### SAFETY TESTS

As they are of unusual interest at the present time the safety tests applied to the vaccine will be described in some detail. They are based on, but are not identical with, the minimum requirements of the United States of America Public Health Service for poliomyelitis vaccine. Since the 'Cutter incident', several modifications have been made and the latest regulations are much more comprehensive and stringent than the original version.

The tests of the South African poliomyelitis vaccine are carried out by a separate team under Dr. H. H. Malherbe, who has compiled the following account of them:

#### AMOUNTS OF VACCINE TESTED

The volume of each sample is constant, and is independent of the size of the lot or pool from which it is taken.

#### TESTS CARRIED OUT BEFORE INACTIVATION OF VIRUS

These are performed on unfiltered monovalent-type lots.

##### For *M. tuberculosis*

(a) Four guinea-pigs are each inoculated intraperitoneally with 5.0 ml. of uncentrifuged type lot fluid. They are observed for 42 days, and at least 2 animals must survive for this period. They are then autopsied, and spleens and abdominal lymph-nodes are examined histologically. Animals which sicken or die later than 24 hours after inoculation are investigated to determine the cause of illness.

(b) 15.0 ml. of type lot fluid are centrifuged at 1500×g for 1 hour. The sediment is cultured in 2 bottles of Lowenstein-Jensen medium at 36°C for 42 days. If no growth occurs the bottles are discarded as negative; if growth occurs, it is examined for acid-fast bacilli.

##### For Herpes B virus

Three rabbits are each inoculated with 0.25 ml. of type lot fluid in each of 4 intradermal sites, and with 9.0 ml. subcutaneously. The animals are observed for 28 days, and any which sicken or develop skin lesions are investigated to determine the cause of illness. At least two rabbits must survive the test period. Material suspected of containing herpes B virus is sub-inoculated into rabbits, as well as into monkey kidney and chick embryo tissue-cultures.

#### TESTS CARRIED OUT DURING INACTIVATION OF VIRUS

These are performed on filtered monovalent type lots.

##### Tissue culture

Samples of at least 600 ml. each are taken from type lots during inactivation, with an interval of approximately 3 days between samples. The fluid is dialysed at 4°C to remove free formaldehyde.

Each of 10 bottles with a culture area of approximately 180 sq. cm. each is inoculated with 60.0 ml. type lot fluid and 100 ml. nutrient medium without serum. The bottles are kept for 25-28 days; and every 4-5 days half the fluid in each bottle is replaced with fresh medium containing 0.5% pre-tested horse serum or calf serum.

Sub-inoculations are made at approximately 5, 15 and 25 days; when from each bottle 5.0 ml. of fluid are taken for sub-inoculation. Into each of 5 roller tubes containing 2.0 ml. of nutrient medium without serum, 1.0 ml. of fluid from the bottle is introduced, and after 4-5 days half the fluid in the tube is removed and replaced with fresh medium containing 0.5% pre-tested serum. The tubes are finally read 10 days after inoculation.

At least 8 bottles must survive for 14 days; and any in excess of 2 lost before the 14th day through causes other than poliovirus must be replaced by freshly inoculated bottles.

The test is evaluated on the reading of the sub-inoculation made about the 15th day, provided that poliovirus is not recovered at any stage of the test.

If virus is isolated from a type lot, 2 further samples of 600 ml. each taken during re-inactivation must be tested.

No monovalent-type lot may be incorporated in a trivalent pool unless both consecutive samples taken during inactivation are negative.

#### TESTS CARRIED OUT ON TRIVALENT POOLS

##### Tissue culture

A sample of at least 1,800 ml. of trivalent pool fluid is dialysed to remove free formaldehyde. The sample is divided into 3 parts, each of which is tested on a different tissue-batch. The tests are carried out in the same way as during inactivation of virus, 10 bottles each receiving 60.0 ml. of pool fluid. Not less than 25 bottles must be negative after 14 days, and any in excess of 5 lost before the 14th day through causes other than poliovirus must be replaced by freshly inoculated bottles.

If poliovirus is found in a trivalent pool, the pool may be re-filtered and reheated once, 2 further samples of 1,800 ml. each being tested. Both of these samples must be negative before the pool is released.

##### Mice (for detection of lymphocytic choriomeningitis virus)

Ten or more mice are each inoculated intracerebrally with 0.025 ml. of undialysed trivalent pool fluid. They are observed for 28 days, and any mice which sicken or die later than 24 hours after inoculation are investigated to determine the cause of illness. At least 8 mice must survive the full period.

#### TESTS CARRIED OUT AFTER AMPOULING

##### Monkeys

Twenty vervet monkeys are each inoculated with 2.5 ml. of a sample of vaccine made up from final containers representing all

batches ampouled. Each monkey receives 0.5 ml. bilaterally into the thalamic region, 0.5 ml. into the lumbar cord, and 1.0 ml. into the right gastrocnemius muscle. In addition, each monkey is given 200 mg. of cortisone acetate into the left gastrocnemius muscle, and 300,000 units of procaine penicillin into the right biceps brachii muscle.

Animals which fail to survive the first 48 hours after injection may be discarded and replaced by an equal number. At least 16 monkeys must survive the full period of the test.

The animals are observed for 18 days. Any showing signs of serious illness not responding to additional antibiotic treatment are sacrificed to determine the cause of illness, and specimens of central nervous tissue are taken for virus isolation and for histological examination.

A minimum of 5.0 ml. of blood is taken from each animal on the following occasions: (1) Before inoculation, for serological tests; (2) on the 4th day after inoculation, for virus isolation; (3) on the 7th day after inoculation, for virus isolation; and (4) at the time of sacrifice, for serological tests.

Serological tests are performed on all pre-inoculation sera; but are done on paired pre- and post-inoculation sera only if histological lesions are found.

The sera are diluted 1 : 4 (final) and are tested against 100 TCID<sub>50</sub> of the 3 poliovirus types.

Animals which survive the 18-day period are sacrificed and the following specimens taken:

1. Blood for serological studies.
2. Tissues for virus isolation: (a) A 1 sq. cm. block of cortex at the site of inoculation on one side; (b) the upper part of the cervical cord enlargement, comprising segments C2, 3 and 4; and (c) the upper part of the lumbar cord enlargement, comprising segments L2 and 3. These tissues are pooled and stored at -20°C. and are used for virus isolation if histological lesions are found.

3. Tissues for histological study: (a) Medulla, including the area postrema (one tissue block); (b) the lower part of the cervical cord enlargement, comprising segments C5, 6, 7, and T1 (3 tissue blocks), and (c) the lower part of the lumbar cord enlargement, comprising segments L4 and 5 (3 tissue blocks).

4. Reserve tissues for histological studies in the event of lesions being observed in the tissues mentioned in the preceding paragraph: (a) Thoracic cord adjacent to cervical and lumbar enlargements; (b) pre- and post-central gyri on one side; (c) parietal, temporal and occipital cortex on one side; (d) Corpus striatum; (e) thalamus; (f) midbrain; and (g) floor of the widest part of the fourth ventricle, with the cerebellum overlying it.

Samples of sera taken from all monkeys on the 4th and 7th days are tested for the presence of virus. Each of 10 roller tubes is inoculated with 0.1 ml. of serum, and the tubes are observed for 14 days.

Typical distribution of characteristic lesions of poliomyelitis in brain and cord is adequate evidence of infection with poliovirus. In doubtful cases, the histological evidence will not be considered final; the ultimate conclusion being based on the combined results of virus recovery attempts, serological studies on paired sera, and a careful review of the nature and distribution of the lesions observed.

#### Guinea-pigs

A test for toxicity is done by inoculating each of 4 guinea-pigs intraperitoneally with 5.0 ml. of ampouled vaccine. Temperatures are taken daily for 10 days, and should not reach 104°F or over. The test may be repeated once only.

#### ORGANIZATION OF THE VACCINATION CAMPAIGN

The first batches of poliomyelitis vaccine were ready for issue early in 1955. The Minister of Health assumed responsibility for the control of the issue of this vaccine. He appointed a Committee of experts to advise him on this and other matters pertaining to the vaccine. The first meeting of the Committee was held in April 1955. At this meeting after reviewing all the information available, it was decided to postpone the issue until the report of the Vaccine Evaluation Committee, headed by Dr. Francis on the results of the large-scale

trial conducted by the National Foundation for Infantile Paralysis in the United States in 1954, was available. This was due for publication in mid-April. At the next meeting of the Committee held at the end of April the Francis Report was considered. This document reported that the vaccine was safe and effective. However, on the same day reports of cases of paralytic poliomyelitis following the use of recently released vaccine were received. In view of these disquieting reports the Committee again recommended that the vaccine issue should be postponed until the situation was clarified. In the meantime, it was recommended that all the vaccine prepared in South Africa should be re-submitted to the safety tests. This was done.

In August, soon after the report of the investigating Committee of the United States Public Health Service was received, another meeting of the Committee was called. At this meeting it was reported that the vaccine available for issue had been re-tested and found again to conform to the minimum requirements of the United States Public Health Service. It was also reported that amongst about 5,000,000 American children vaccinated since May, there had been no untoward incidents and that in Canada about 900,000 children and in Denmark 400,000 children had been vaccinated with no untoward incidents. In view of these more recent and encouraging reports, and in view of the fact that the proportion of the South African vaccine which had been tested was far in excess of that demanded in the minimum requirements in the United States, the Committee after long deliberation recommended to the Minister that the vaccine should be released for issue. The Minister, who accepted this recommendation, communicated his decision to the public by the quickest channels, the daily press and in the radio news. Parents who wished to have their children inoculated were invited to send in their names and ages to their medical practitioner or to their municipal health department. A list of these applications was then submitted to the Poliomyelitis Research Foundation.

In view of the uncertainty about its safety, caused by the 'Cutter incident' in the United States and some adverse local criticism, it was not anticipated that the demand for vaccine would be great. However, the demand exceeded the supply available. The Minister of Health then appointed a Priorities Committee to advise on the allocation and issue of the vaccine. It was decided that this should be restricted to children under the age of 6, and children of doctors and nurses up to the age of 16 years.

Arrangements were then made for the issue of the vaccine by the South African Institute for Medical Research directly to the health departments and medical practitioners concerned. The vaccine was sent under refrigeration to its destination. Approximately 16,000 doses were issued. It is estimated that about 15,000 children were vaccinated. It was decided to submit the second batch of vaccine, destined for the second dose, to the latest minimum requirements of the United States Public Health Service, which were published after the batch was ready for issue. In attempting to do this, difficulty was experienced with dialysis and the tests could not be completed. It was then decided to

postpone the issue of the second dose until the winter of the next year.

#### RESULTS OF THE VACCINATION

##### Reactions following vaccination

No cases of paralytic poliomyelitis attributable to the vaccine were notified. Two cases of erythematous skin-rash, probably allergic in origin, were reported. Two children who developed an acute febrile illness within a week of receiving the inoculation were thoroughly investigated. One of these was admitted to a fever hospital, where he was found to be suffering from bacterial gastro-enteritis. The other was found to have an acute haemolytic streptococcal infection of the throat.

Two sisters complained of numbness and weakness of the legs the day after the inoculation. It was concluded finally that this was of psychological origin.

##### Immunity response in human beings

All batches of vaccine, before issue, are required to be potent as shown by the production of antibody in inoculated animals. The batches of vaccine which were issued, and those which will soon be issued, have been shown to be antigenic in either monkeys or guinea-pigs, or both. It is desirable that they should also be shown to stimulate the production of antibody in inoculated children.

No large-scale tests have been made in South Africa to determine the immune response of inoculated individuals. However, the results of two tests will be given to indicate that the vaccine does stimulate the production of antibodies in inoculated individuals.

The results of immunity tests in 5 of 12 individuals given 2 or 3 injections of the vaccine before its release for general issue are given in Table II. These results indicated that the vaccine stimulated the production of antibody of the types which were absent in these subjects, except in the case of 2 subjects who failed to develop Type-3 antibody. The other 7 subjects inoculated, the family of a member of the staff of this institution,

TABLE II

Subject No.	Age (years)	Before inoculation			After inoculation		
		T1	T2	T3	T1	T2	T3
1 .. ..	48	+	+	-	+	+	+
2 .. ..	10	-	+	-	+	+	+
3 .. ..	7	-	+	-	+	+	+
4 .. ..	5	-	-	-	+	+	+
5 .. ..	13	-	+	-	+	+	-

+ = Protection. - = No protection.

were found to have all 3 poliovirus antibodies in their pre-inoculation specimens of serum as well as in the post-inoculation specimens.

Dr. J. P. de Villiers, Medical Officer of Health of the Cape Divisional Council, arranged that a group of 60 school children should be tested before and after a course of 2 inoculations of vaccine, with an interval of 6 weeks between them. Most of these children, before vaccination, were found to have one or more poliovirus antibody types. Many had antibody against all 3 types

TABLE III.

Subject No.	Before inoculation			After inoculation		
	T1	T2	T3	T1	T2	T3
1 .. ..	+	+	+	+	+	+
2 .. ..	-	-	-	+	+	+
3 .. ..	-	-	+	+	+	±
4 .. ..	+	-	-	+	+	±
5 .. ..	-	+	+	+	+	+
6 .. ..	+	+	+	+	+	+
7 .. ..	+	-	-	+	+	+
8 .. ..	-	+	+	+	+	+
9 .. ..	+	+	-	+	+	+
10 .. ..	+	-	+	+	+	+

of poliovirus. However, of those tested who lacked antibody against 1 or more types before vaccination, all except 1 developed antibody against all 3 types of poliovirus after vaccination. The results of the tests on 10 of these children are given in Table III.

#### EFFECTIVENESS OF VACCINATION

The number of children inoculated is too small to permit of definite conclusions regarding the protective value of the vaccine. However, some observations of interest have been made.

During the succeeding autumn, poliomyelitis became epidemic in the Transvaal and in East London. During this time 3 cases of suspected poliomyelitis was notified in children who had been vaccinated. The first occurred in March at Johannesburg in a 5-year-old child, who had received 2 inoculations of vaccine in the preceding September and October respectively. After a febrile illness he developed facial weakness on the left side. This was transient, lasting less than a week. A lumbar puncture revealed that the cerebrospinal fluid was normal. Throat swabs, rectal swabs and faeces were examined in tissue culture for the presence of poliovirus. These tests gave negative results. There is thus doubt about the cause of his illness.

The second case was reported from Cape Town. This was a Coloured infant 18 months old, who had received one injection the preceding September. In March after a febrile illness he developed flaccid paralysis of the right leg. This clinical picture clearly suggested poliomyelitis. However, a lumbar puncture revealed a normal cerebrospinal fluid and poliovirus was not isolated from a specimen of faeces. Doubt therefore remains as to the true aetiology of this case too.

The third case affected a 5-year-old girl, who received one injection of poliomyelitis vaccine the preceding September. This case was notified in April by the Medical Officer of the Peri-Urban Areas Health Board and was admitted to the Boksburg-Benoni Hospital, where she was found to have weakness of the back. The first lumbar puncture showed the presence of 16 lymphocytes. A second lumbar puncture showed the presence of 2 polymorphonuclear leucocytes and 3 lymphocytes and a raised protein-content. Again the clinical picture is suggestive of poliomyelitis, but poliovirus was not isolated from the specimens of enema washings and faeces submitted to the Laboratory. Doubt therefore arises as to the cause of this case as well.

The experience of 4 particular families is also of

interest. In the first, with 4 children, 2 of whom were vaccinated and 2 were not, the 2 who were not vaccinated were admitted to hospital with paralytic poliomyelitis and one required respirator treatment for 4 weeks, and the 2 vaccinated children remained well.

In the second family there were 3 children, of whom one was not vaccinated and developed paralytic poliomyelitis and required respirator treatment for 3 weeks. The other 2 children, who had been vaccinated, remained well.

In the third family, of 2 children, one was vaccinated and the other not. The unvaccinated child developed paralytic poliomyelitis. Her vaccinated sister remained well.

The fourth family consisted of 4 boys, all of whom were vaccinated. Before vaccination the elder 2 boys had antibody against Type-2, but not against Type-1 and Type-3 poliovirus. The third had no demonstrable antibody. The youngest was not tested. After vaccination the elder 2 developed antibody against all 3 viruses. The third developed antibody against Type-1 and Type-2, but not definitely against Type-3 poliovirus. Two years later all 4 came into contact with a case of poliomyelitis. The two elder boys developed no signs of illness. The two younger developed an abortive illness, and continued to excrete Type-1 poliovirus for several weeks. Vaccination therefore did not protect them from infection; it may have helped in preventing paralysis.

Obviously not much significance can be attached to these family infections. However, if the paralytic cases had been in the vaccinated children and the unvaccinated children had remained well, the incidents would have been disturbing.

#### SUMMARY

The preparation of poliomyelitis vaccine in the Laboratories of the Poliomyelitis Research Foundation of Southern Africa is described. In general the methods adopted follow those described by Salk and his associates. However, the strains of virus used to represent

the 3 types of poliovirus in the vaccine are different, and the ones recently incorporated, obtained from Dr. A. B. Sabin, are relatively non-virulent. The method of inactivation with formalin has been slightly modified and, in recently prepared batches, has been supplemented by treatment with ultra-violet light. These modifications were introduced to ensure greater safety.

Before issue the vaccine is required to conform with the minimum standards for potency and safety laid down by the Union Health Department. These are based on the latest minimum requirements for poliomyelitis vaccine of the United States Public Health Service.

No serious untoward reactions occurred in about 15,000 children inoculated with the South African vaccine in 1955. This number is too small to base conclusions on concerning the value of the vaccine in preventing paralytic poliomyelitis. During the epidemic which occurred in the following autumn of this year 1956, there have been amongst the vaccinated children 3 suspect cases of paralytic poliomyelitis, but from none of them was the poliovirus isolated. In 3 families in which some of the children were vaccinated and others not, the unvaccinated children contracted paralytic poliomyelitis and the vaccinated children remained well. This occurrence is probably not significant. It has been shown that previous vaccination does not necessarily prevent infection with poliovirus. It may lessen the liability to paralysis, but further observations are needed to determine how long this protective effect will last.

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### INTERNATIONAL CANCER CYTOLOGY CONGRESS

The First International Cancer Cytology Congress, sponsored jointly by the International Union against Cancer, the College of American Pathologists, the American Society for Clinical Pathologists, and the Inter-Society Cytology Council, will be held at the Drake Hotel, Chicago, Ill., USA on 9, 10 and 11 October 1956.

Panel discussions will take place on the following subjects: Aspiration biopsy; Problems in confirming cellular evidence of cancer; Prognosis in cancer of the uterine cervix as determined by histologic and cytologic methods.

The subjects of papers to be submitted are as follows: The historical landmark in exfoliate cytology; The present-day scope of clinical cytology; Structure of the fixed and stained cell; Possibly distinctive properties of malignant cells; Normal cells originating in respiratory tract; Pulmonary cancers and their cells—a study of sputum; Pulmonary cancers and their cells—a study of bronchial washings; The cellular content of effusions not related to cancer; Recognition of malignant tumour cells in effusions; The

cellular detection of carcinoma of the esophagus; Normal and abnormal cells in gastric washings; The cellular detection of cancers involving the urinary tract; A pathologist's view on the subject of cytology; Problems in mass screenings; The automatic scanner; Normal cells arising in the female genital tract; Metaplasia of the uterine cervix; Atypia of the uterine cervix and its relation to trichomoniasis; 'Pre-cancerous' changes in the uterine cervix; Cellular changes simulating those of cancer; Cellular study of epithelial dysplasia in pregnancy; Squamous cell cancer of the uterine cervix—a histocytological study; The cellular detection of uterine adenocarcinoma; New advances in cytology (papers to be selected).

A symposium will also be held on carcinoma in situ of the uterine cervix.

Further information can be obtained from Professor J. Gillman, Chairman, Subcommittee on Cancer Detection, International Union against Cancer, Department of Physiology, Medical School, Hospital Street, Johannesburg.

## THE PHENOMENON OF GLAUCOMATOCYCLITIC CRISES

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It was in April 1952 that Frederick H. Theodore of New York, writing in the *British Journal of Ophthalmology*, emphasized the importance to ophthalmologist and patient of recognizing this fascinating syndrome, first adequately described by Adolf Posner and Abraham Schlossman of New York in 1948. Even today its importance is not fully recognized and indeed it is described in extremely few of the text-books of ophthalmology.

I have seen 3 cases in the last 18 months, but particular interest was stimulated by a case I recently saw in Johannesburg. This case presented some features which to my knowledge are not mentioned in the literature. I was fortunate in obtaining a very accurate history, extending back 2 years, from the patient's husband, who is an experienced medical practitioner. Before describing the case I shall give a brief resumé of this clear-cut syndrome.

*Gross Diagnostic Characteristics*

The name is well chosen and represents the main features, namely, (1) raised intra-ocular pressure varying from 30 mm. to 90 mm. Hg, (2) evidence of cyclitis which is, however, confined to large, flat, white keratic precipitates (KP) and occasional cells in the anterior chamber and, (3) recurrent attacks of acute onset which always affect the same eye, the syndrome being strictly unilateral.

*Additional Features*

It is extremely rare in acute glaucoma (a) to get repeated attacks with no concurrent deterioration of the visual fields or cupping of the optic disc. (b) It is equally rare to get a high intra-ocular pressure with such little deterioration of visual acuity during an acute attack. (c) It is practically unknown for acute congestive glaucoma to subside spontaneously without treatment. These 3 features, however, are seen in glaucomatocyclitic crises and they are the points which provide the finesse in the diagnosis of this syndrome. Between attacks no evidence of previous ocular disturbance is seen and all provocative tests for glaucoma are negative, no signs of previous cyclitis being present. Paradoxically the treatment most effective in acute glaucoma is least effective in the treatment of this syndrome, since Diamox and meiotics have no effect and surgical intervention has never once been reported to control the attacks; indeed it is strongly contra-indicated. Mydriatics often increase the symptoms and raise the pressure.

## CASE REPORT

*Past History*

In December 1953 the patient, a lady then aged 24 years, experienced her first attack. It began with a burning sensation in the left eye, blurring of vision and definite coloured haloes around lights. The doctor husband, taking these symptoms into account and noticing the left pupil larger than the right and feeling the

pressure in the eye to be raised, diagnosed glaucoma and immediately put eserine drops into the eye. Although the pupil soon became pin-point in size, the symptoms remained unchanged, and the following day an ophthalmologist was consulted. His diagnosis was iridocyclitis with keratic precipitates and he prescribed 1% atropine drops. The attack finally cleared up after 3 weeks.

In an endeavour to locate a possible trigger focus, the patient's teeth, sinuses and chest were X-rayed and a Wassermann test and full blood-count and urinalysis performed. The results were all within normal limits. The ophthalmologist advised the patient to carry 2% homatropine constantly and instill it immediately if symptoms recurred. This opportunity arose 2 months later when a similar attack occurred. This attack was treated with the homatropine drops and cleared in 2 weeks.

The patient had for many years suffered from pyelitis with her menstrual periods and a particularly bad attack occurred soon after her second ocular episode. A urologist was consulted, who advised a right nephropexy to abolish a definite kinking of the right ureter shown on intravenous pyelogram, because it was felt that the chronic pyelitis might have had some effect on the iridocyclitis.

A right nephropexy was performed, and it was indeed disappointing when the third ocular episode occurred only one month afterwards, in March 1954, and the fourth and fifth attacks in May and August 1954, all affecting the left eye. These attacks lasted about 2 weeks and were treated with homatropine 2% drops. The husband and wife moved to the Orange Free State and after a 6 months' period free of symptoms, the sixth left ocular attack occurred. Haloes were a particular feature this time and after an attack of almost projectile vomiting at 2 a.m. an ophthalmologist in the vicinity was consulted.

He diagnosed acute congestive glaucoma and said there were no signs at all of previous iridocyclitis. The Schiotz tenometer reading was L.E. 45 mm. Hg and R.E. 20 mm. Hg. An intensive course of 1% eserine brought no relief and 24 hours later the Schiotz reading remained unchanged. Diamox and eserine were then combined and, although side-effects of paraesthesia of the fingers and feet were produced, the symptoms and signs were unaffected and after 3 days the tension was 50 mm. Hg in the left eye and remained so for the next 5 days. The ophthalmologist now advised a drainage operation as the only alternative. As a last resort the husband decided to try an idea of his own. He produced a marked diuresis by giving his wife large doses of ammonium chloride followed by an injection of 2c.c. of Mersalyl. The patient felt much better the following day and for the first time in 2 weeks the tension in the left eye had fallen to 25 mm. Hg (Schiotz). On this occasion the ophthalmologist suggested using neocortef ointment to treat the patchy shredding of oedematous corneal epithelium. Three days later all signs and symptoms had disappeared. Three months later, when back in Johannesburg, the patient had an allergic reaction to an intramuscular injection of 100 mg. of Pethidine given for the treatment of a miscarriage. This manifested itself as oedema glottidis and slow respiration, but recovery was satisfactory. The seventh attack in the left eye began soon after this allergic episode and another ophthalmologist was consulted. He diagnosed acute congestive glaucoma and commented that there were no signs of any previous iridocyclitis. He prescribed 1% pilocarpine drops, 4 hourly. Mersalyl was again tried and that night 2 c.c. were given intramuscularly. The next morning symptoms had lessened and the tension was reported to be normal. All signs and symptoms disappeared within the next 3 days.

This story of medical misfortune was soon to be continued, for after taking 2 aspirins for dysmenorrhoea while on holiday in Rhodesia, the patient developed the worst urticarial rash the husband had ever seen. Luckily, however, there was a rapid response to ACTH. The eighth left ocular attack occurred soon after their return to Johannesburg and another ophthalmologist's opinion was sought. He thought acute congestive glaucoma to be the basis of the trouble and prescribed 1% pilocarpine drops 4 hourly. On a second visit 5 days later he saw keratic precipitates and changed his diagnosis to secondary glaucoma. The visual

fields were tested and found normal and the attack had cleared in another 5 days.

#### *The last two Attacks*

At 11.30 p.m. in mid-December 1955 I received a telephone call from the husband, who explained that his wife had nausea and was seeing haloes with her left eye. I examined her about an hour later.

**On Examination.** Unaided vision of right eye 6/9, left eye 6/12. There was a partial ptosis of the left upper lid and slight swelling of the lateral part of both the left upper and lower lids. There was mild congestion of the conjunctival vessels. The cornea appeared bright, but some small white specks could be seen naked-eye, just below the centre of the cornea. The pupils were equal in size and the pupillary reflexes were normal. There was no heterochromia. The media, discs and fund were normal.

**Slit-Lamp Examination.** The cornea showed no evidence of oedema. There were 8 white, flat, discrete, irregular keratic precipitates, all aggregated in a small area about 2 mm. below and slightly nasal from the centre of the cornea. Occasional cells were seen in the anterior chamber, but no flare. The pupillary margins of the iris and the anterior lens-capsule were normal and showed no signs of past or present iridocyclitis.

**Visual Fields and Tension.** The visual fields were full and normal. The tension was 20 mm. Hg (Schiotz) in both eyes. Since I felt sure the diagnosis was glaucomatocyclitic crises, I prescribed cortisone ointment 1.5% hourly. Two days later the KP began to fade and 3 days after commencing treatment the left eye was normal. The vision was now 6/6 R and L the eyes appeared normal on examination. The tension was measured many times during this attack, and was always found to be normal.

The missing link in the diagnosis, namely a proven raised tension, was provided by the next attack some 5 weeks later. I then saw the patient at 5 p.m. on 26 January 1956, 12 hours after the attack had begun. Haloes were a predominant symptom.

**On Examination.** Right eye, vision 6/6, normal on examination; left eye, vision 6/9.

**Examination of Left Eye.** There was a slight drooping of the left upper lid. Ocular movements were full and normal. The moderately congested conjunctival and ciliary vessels had a definite cyanotic tinge. The periphery of the cornea appeared dull, but the centre part was normally bright. In exactly the same position as before, the little white specks could be seen. The left pupil was slightly larger than the right, and was round but sluggish in its reaction to light and accommodation. The media, disc and fundus were normal.

**Visual Fields and Tension.** The visual fields were full and normal. The tension was 45 mm. Hg (Schiotz). (The right tension 20 mm. Hg.)

**Slit-Lamp Examination.** The right eye was normal. The left eye showed a peculiar corneal oedema confined to the periphery of the cornea and especially clustered in blebs around the loops of the limbal vessels. This was particularly noticeable on the medial side opposite a moderately vascular pinguecula. There were 9 large white flat discrete keratic precipitates in exactly the same position as in the last attack, and some peppering with minute precipitates of the small area between the closely aggregated keratic precipitates. There were occasional cells in the anterior chamber, but no flare. Iris and lens were normal.

**Treatment and Result.** 26 January: Cortisone, 1.5% drops, was started immediately in the left eye and instilled every 5 minutes; after 2 hours 1.5% cortisone ointment was used and the patient went to bed.

27 January: Symptoms and signs about the same, the tension of the left eye now being 36 mm. Hg.

29 January: The symptoms were still present and the patient had vomited at about 2 a.m. The keratic precipitates were beginning to fade, but the tension was still 40 mm. Hg (Schiotz). The husband suggested using Mersalyl and we gave the patient 2c.c. intramuscularly.

30 January: The patient volunteered that in the morning she had felt a peculiar sucking sensation in the eye. After this all symptoms disappeared. In the evening, the complete metamorphosis was striking, for now the left eye was completely

normal. The tension was 20 mm. Hg in both the right and left eyes and the visual fields full and normal.

#### DISCUSSION

Here indeed is a fascinating case of the syndrome of glaucomatocyclitic crises with a 2-year history. During this time 10 attacks were experienced, the last 2 being observed by the author. It appears from the history and findings of colleagues that the syndrome was sometimes predominantly glaucomatous in appearance, with accompanying symptoms of haloes, burning of the eye and, on two occasions, projectile vomiting, whereas on other occasions the appearance was one similar to cyclitis with no raised tension.

**Treatment.** Although Diamox, eserine, pilocarpine, homatropine and atropine were all used on different occasions, the only effective remedy in shortening an attack appears to be cortisone, and especial note should be taken of the dramatic effect of the diuresis produced by Mersalyl if the tension is raised, aborting the attack and lowering the tension almost immediately to within normal limits.

**Etiology.** It is tempting to postulate on an allergic basis, as previously suggested in the literature, to account for these attacks. Supporting evidence is undoubtedly the acute onset and cessation, the self-limited attacks, an allergic history of the patient and a strong family history of allergy. The slit-lamp appearances of oedema localized to the vicinity of the limbal loops and the slight swelling of the lids with slight ptosis all support this hypothesis of an allergic reaction, with vascular dilatation and oedema. The keratic precipitates are peculiar, for their position was the same in each attack observed by me—they are closely aggregated together and hence do not appear to be deposited according to the influences of gravity, convection currents or generalized corneal endothelial disturbance. They never become pigmented, and disappear without leaving a trace. Their usual flat and white appearance suggest that they are not formed by inflammatory cells and debris adhering to the damaged endothelium, but are possibly protein products, the result of an allergic vascular intra-ocular anomaly. Indeed if the angle was blocked by oedema, it might well explain the dramatic effect of Mersalyl in carrying away the oedema, and the apparent lack of effect of Diamox, so useful in most types of glaucoma, since the action of Diamox does not seem to depend on its diuretic properties, but more on its effect on carbonic anhydrase, bicarbonate secretion into the eye and intra-ocular fluid production.

In the few cases reported on which surgical drainage operations were performed, no relief from attacks was obtained—very different from our experience of ordinary acute congestive glaucoma. It is puzzling that although the tension may remain high for as long as 2 weeks, no deterioration is seen in the visual field and no atrophy or cupping of the optic disc.

#### SUMMARY

A detailed history and case report of a patient suffering from glaucomatocyclitic crises is given. Treatment and

etiology are discussed and emphasis laid on the importance to patient and ophthalmologist of recognizing this syndrome as a distinct clinical entity. Cortisone is the treatment of choice in cases predominantly cyclitic, whereas cortisone eye-ointment and Mersalyl

intramuscular injection appear most effective if the pressure is raised.

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### AN INTERN'S REFLECTIONS

H. E. CLIFFORD, B.Sc., M.B., Ch.B., (Cape Town)

The regulations governing internships prescribe that the intern should have time for reflection. Since little opportunity for this luxury was afforded me during my internship I have taken the liberty of spending a few hours in constructive reminiscence now that the year is done.

My internship was unusual in that it was divided into two terms of extreme contrast—in a teaching hospital and in an isolated mission hospital in 'virgin soil'. Witnessing these two diverse forms of medical practice has left me with an impression of the virtues of each and an understanding of the place of each in the profession and in the community. It has given me what I sought most—a sense of balance and perspective to guide me as I enter into practice myself.

#### TWO CONTRASTING PRACTICES

In my humble yet privileged post in the teaching hospital I was associated with about 40 other interns and perhaps 5 times as many doctors of much higher qualification. Specialists and authorities abounded, and were readily available for consultation. As far as I was concerned, real problems did not exist, for when they arose they could be delegated to someone more qualified than I to solve them.

Besides this assistance in the clinical sphere there were the medical personnel and technicians attached to the diagnostic departments—pathology, radiology, and more circumscribed fields such as electrocardiography, angiography, plethysmography... All of these services were available to add confidence, and a degree of absolute certainty, to the clinical diagnosis.

The diagnosis having been established, treatment was instituted on the sole basis of efficacy and convenience. An efficient pharmacy apparently (if not actually) unencumbered by financial considerations and wholly devoted to dispensing, operated under the same roof, and catered for the most enthusiastic, exacting, or generous physician. One could prescribe the best for the poorest patient with the abandon with which one enjoys any item that is 'on the house'.

One may wonder why an intern working under such luxurious circumstances should choose to transfer to a humble mission hospital where financial considerations dominated the management of every patient.

This hospital, serving a community of Native villages up to 75 miles distant, boasts two doctors, a hundred beds, and eight thousand out-patients a year. There are medical, surgical, obstetrical, and pediatric departments, but the divisions are artificial except for accommodation, for the same staff operates all departments; and the medical and surgical departments include all the specialties.

The range of conditions encountered was as great and varied as in a large city institution, but there were no avenues of delegation or reference. Diagnosis was mainly clinical, aided by simple 'side-room' investigations. Treatment was a compromise between economy and efficacy, and ways and means of satisfying both *desiderata* were fully explored. It is remarkable what can often be accomplished by adding a little trouble to simple measures, in exchange for an easier way at higher cost.

#### CONTRASTING VIRTUES

In the large teaching institution I witnessed the most advanced, the most scientific, the most thorough and the most generous medical practice. Herein for me lay one great virtue and one great drawback. The virtue was that a high standard was set

before me—an ideal, something which I could not practice in its fullness myself, but could strive towards. The importance of a critical outlook, and of accuracy, was impressed upon me. I was taught to develop an objective approach to medicine, and to rely on facts rather than on feelings and impressions. Professional honesty was regarded as supreme. It was good discipline, and good discipline is invaluable to the practice of good medicine. Of all the lessons I have learned since I began medicine as a student, perhaps this is the most important.

If the virtue lay in what I learned from observation, the drawback lay in what I lost through lack of personal experience. Simple technical procedures only were left to me. Decisions of moment were made by others. Administrative problems were dealt with by a separate staff entirely. Finally, even my own movements were not spontaneous, but were closely directed by others. Thus the indispensable virtues of dexterity, discretion, economy and individuality had little chance to develop.

In the smaller institution I entered the practice as an apprentice-partner. I was trained to share the work and responsibilities and, if necessary, carry them entirely for short periods. This forced me to apply myself to the practical issues of medical practice, including surgery. This latter, so exclusively guarded in training institutions and specialty practice, I found to be amenable in part to inclusion in a general type of practice.

My chief was a general practitioner of innate and cultivated dexterity; his local renown was a testimony to his work. Under his guidance I learned to do what he did—the common operations in general surgery, and some usually included in specialist departments.

Modern trends in medicine lean towards ever-increasing departmentalization and specialization, and the sphere of the general practitioner is gradually becoming more circumscribed. While this is to a certain extent inevitable, I cannot but feel that the rightful status of the specialist—as a consultant rather than the exclusive practitioner of his sphere of medicine—should not be lost sight of; and that the dexterous and experienced general practitioner is still the ideal agency for the practice of medicine in the community today.

#### Perspective and Practicability

I chose to transfer to a mission hospital for part of my training for two main reasons: (1) Because medicine as practised in a large departmentalized institution is not wholly practicable at the domestic level, and (2) spiritual and social ideals of medical practice tend to be lost sight of in the environment of a large specialist hospital.

Just as difficulties, fallacies and exceptions tend to be overlooked in general practice for the sake of convenience and economy, so they tend to be exaggerated in specialist practice for the sake of precision. The general practitioner's method is based on probability, and it is fortunate that the vast majority of pathological conditions can be diagnosed clinically with an acceptable degree of accuracy. I say fortunate because the clinical method is adaptable, economical and simple. To make medicine a more exact science, clinical methods are supplemented by physical and chemical methods which, though frequently precise and objective, are often elaborate, unadaptable and expensive. In specialist practice the indispensability of these methods is impressed upon the intern. I recollect being told once that 'no cardiac condition can be adequately diagnosed and treated without an ECG'. Statements and teachings such as this tend to distort the perspective of the beginner in medicine and lead to distrust of the

clinical method which is unfortunate, for the clinical method is, and probably always will be, the sheet anchor of medical practice.

It is easy in circumstances where special investigations are readily available, to apply them more generally than might be necessary. They become items of adornment rather than of utility. This tendency to 'window-dressing', as one teacher expressed it, is becoming too common in medical practice today. It is a danger to universal good practice because (1) it is expensive; (2) it is attractive to the layman, and may be exploited by the mercenary; (3) it tends to become a substitute for, rather than a supplement to, critical clinical observation.

#### *Social and Spiritual Ideals in Practice*

Enlightened men in every walk of life today visualize something greater in their occupations than the mechanical accomplishment of their task. Higher ideals than material or mere academic attainments and gains should motivate one's life and work.

Social medicine is an organized attempt to apply this philosophy to medical practice. Social medicine seeks to serve the needs, problems and interests of the community. Though it can be taught in universities and demonstrated in large institutions, the general practitioner is the medium through which it must be applied to the nation. Health education, maternal and child welfare, and a healthy attitude towards disease by laymen, can all be most effectively taught and promoted by the practitioner at the domestic level.

As a student one is often enjoined to 'treat the patient as a whole', yet the fullest expression of this injunction is seldom appreciated even by those who teach it. True, if a patient has diabetes, one should examine the eyes for retinopathy, the limbs for neuropathy or vascular disease, the chest for tuberculosis, the abdomen for evidence of liver or pancreatic disease, and the urine perhaps for a nephrotic lesion. Yet when every physical system has been thoroughly examined only part of 'the patient as a whole', has been studied. There are social and psychological aspects to the case. Has the impact of the disease on the patient, his family, and his livelihood been considered? Has the patient's reaction to his illness been observed and guided along healthy channels? Has his illness affected his emotional stability or his spiritual integrity?

Every illness influences the patient's psyche to a greater or lesser extent, and often the practising doctor witnesses experiences which must profoundly, and often dramatically, influence the outlook of his patient. In this field there is an urgent, supremely important work to be done. The reward is the satisfaction of seeing a patient well adapted to his illness. This is almost as great as the satisfaction of seeing a patient respond to well-advised treatment.

Illness, especially when associated with distressing circumstances, is an occasion of great spiritual need for the patient. A tactful instilling of confidence at a time like this is a powerful adjunct to successful therapy. In a large departmentalized institution little opportunity is afforded one to learn this aspect of the healing art. There is so much delegation of responsibility that the same degree of confidence and liaison can scarcely be established as when one doctor is the patient's sole confidant. During the second half of my internship I was impressed with the potential of a spiritual liaison with the patient. It aids the doctor by increased patient-confidence and thus a greater revelation of the patient and his disease. It aids the patient by dispelling fears and imparting a sense of trust and security, and adding hope to what might otherwise be a dismal outlook.

Success in medical treatment cannot be gauged by temperature charts, ECGs and ESRs alone; the patient's attitude towards his illness must also be taken into account. A discouraged or disgruntled patient is a failure by any standard, while a patient with a cheerful, understanding outlook, especially against great odds, is a refreshing person to meet and a reflection of good treatment of the patient as a true whole.

The part played by religion in doctor-patient relationships should not be overlooked. Those who practise it are conscious of the great power of religion to direct the attitudes and sentiments of people. It has tremendous potential when allied with the healing art. Even a time of crisis can be made sublime by those of religious persuasion. The Psalmist appreciated the sustaining power of religious faith when he wrote, 'Yea, though I walk through the valley of the shadow of death, I will fear no evil, for thou art with me' (Ps. 23 : 4).

## SUPERVOLTAGE RADIO THERAPY

LIONEL COHEN, M.B., B.Ch. (RAND), D.M.R.T. (R.C.P. & S., ENG.)

*Johannesburg*

A recent paper on *Radio-active Cobalt Bombs and Supervoltage Radiotherapy for South Africa*<sup>1</sup> deals with a subject of vital importance in the treatment of cancer in this country. The undeniable fact that many patients, not excluding doctors, go overseas for treatment, suggests that we are not all satisfied with the standards of radiotherapy now available here. The ideas expressed in this paper are, in fact, at variance with almost all enlightened opinion throughout the world. At the recent conference in Geneva on the peaceful applications of atomic energy, the widespread acceptance of telecurie units for routine radiotherapy, and their many advantages over conventional methods, was emphasized. Indeed, scores of such units have now been mass-produced, and are operating with gratifying success in the USA, the USSR, Canada, South America, Eastern and Western Europe, Australia, India, China and Britain. Is South Africa to be a unique exception?

This form of treatment is opposed on the ground that South Africa, in contradistinction to all other countries in the civilized world, cannot cope with the extraordinary physical and economic difficulties entailed. This may seem to be the case from the point of view of private radiotherapeutic practice, but it should not be so in relation to the very different problems presented by organization and resources in the large Provincial hospital centres. Yet these advanced techniques have, apparently, no place in the type of radiotherapy which, with a few notable exceptions, is currently practised in this country, and which is generally characterized by systematic underdosage.<sup>2</sup>

These considerations confirm the writer's previously expressed view<sup>2</sup> that the highest standards of radiotherapeutic practice can

be supplied only in fully equipped, centrally organized, regional institutions. In such institutions, the use of supervoltage radiation presents no insuperable difficulties, physical or economic, and leads to a definite improvement in the results of treatment, not only in that certain patients who would not have responded to conventional radiotherapy can be cured, but also in that a large proportion of patients curable by conventional radiotherapy would be spared many of the unpleasant reactions and complications unavoidable with conventional radiotherapy. It is obvious, therefore, that there is need to consider these recent developments from the point of view of the current and future requirements of the Provincial hospitals.

#### CLINICAL CONSIDERATIONS

While palliative treatment is still an important, though diminishing, part of radiotherapeutic practice, it is in the effort to increase the proportion of permanent cures that the development of the new techniques and equipment is being pursued.<sup>3</sup> It has been shown,<sup>4</sup> that the curability of the larger and less accessible tumours is limited by the feasibility of delivering large doses to the tumour relative to that received by overlying skin (heterogeneity factor), and by the relative tolerance to radiation of the tumour and the host (therapeutic ratio). Both these factors improve progressively as the energy or exciting voltage of the beam is increased, and reach a theoretical optimum in the 4-million-volt range. With this quality of radiation deep-seated tumours can be treated radically with little or no visible skin-reactions and no risk of

necrosis; systemic reactions are milder, minimizing the nausea, vomiting, diarrhoea and leucopenia which so often prevents completion of a pre-calculated course of treatment; and there is less differential absorption of bone and cartilage, eliminating the complications of chondronecrosis and osteitis in the treatment of tumours of the mouth, head and neck, breast and pelvis. In fact with any tumour extending more than 5 cm. below the skin, and in any situation where bone or cartilage is traversed by the beam, i.e., in about half of all tumours seen in South African hospitals, supervoltage therapy has very material advantages. In fact the improvement is much greater than published figures show, since cancer statistics based on 5-year and 10-year cure rates always lag behind the best results being achieved.

It may be predicted, therefore, that with the exception of non-malignant conditions, skin lesions and the radiosensitive sarcomas, all radiotherapy will, in the very near future, be conducted with megavoltage and telecurie equipment. Such developments in cancer therapy inevitably demand large regional centres fully staffed and equipped to handle the new techniques.

Under conditions currently prevailing in Johannesburg, for example, it is estimated that the most efficient service, from both clinical and economic considerations, would be given by two supervoltage units: one, a 4 MeV linear accelerator, primarily for high-output and large depth-dose treatment to deep-seated tumours, but also adaptable to cases in the other category; and the second, a 1,000-curie unit using cobalt-60 in the first instance for high-quality irradiation of the bony and cartilaginous regions of the head and neck, but adaptable as an alternative to the accelerator if required. The relatively low-dosage output of the telecurie unit is compensated for by the continuous activity of the source, so that by the organizing of 8-hour shifts the normal working turn-over of patients can be tripled without any additional strain on the equipment. The two units, though each ideally suited for specific depth and quality problems, would thus be interchangeable if required should one be out of action for repairs or adjustments.

#### TECHNICAL AND ECONOMIC ASPECTS

Objections raised on account of expense, housing, staffing, running costs, and physical peculiarities of the materials, have all been overcome overseas, and could easily be solved in the larger Provincial hospitals of this country. In South Africa about 10,000 new cancer-cases requiring therapy occur each year, and each of the 6 existing major radiotherapy centres copes with from 1,000 to 1,500 cases annually, of which about one-half would benefit from supervoltage irradiation. The initial cost to each centre of two units totalling, with all the ancillary building and equipment, well under £100,000, can hardly be considered an excessive investment for the treatment of 500 human beings annually, especially as it would be offset by a considerable saving in treatment time and hospitalization expenses. The housing of a supervoltage unit entails concrete walls, floors and roofing up to 1 metre in thickness, obviously prohibitive in a city block of offices, but a simple architectural problem in any central institution designed for the purpose. By suitable siting of a single-story treatment-wing, using outer walls abutting on an unoccupied space or garden, the housing of such units costs no more than that of any conventional X-ray set.

Running costs of telecurie units are negligible apart from replacement of decayed isotope at intervals. Since only part of the source need be re-activated at any one time, a very small fraction of the reactor facility with modern high-neutron-flux piles need be occupied for this purpose, at a correspondingly low cost. In the near future cobalt-60 sources would be replaced with caesium-137, a by-product of uranium fission produced in embarrassingly large quantities by all atomic power plants, which will probably be given free to hospitals and industry to avoid expensive alternative methods of disposal. The long half-life of 33 years makes replacement rarely necessary. These units are fool-proof and require no skilled staff other than radiographers.

With megavoltage generators, at least with the efficient linear accelerators, the high radiation output and rapid turn-over of patients are such that, in a large institution, the running costs are actually lower than that of the several conventional therapy machines that would be required to cope with the same number of cases. Employment of a maintenance engineer may be advisable, but his salary, too, would be offset by the lower running costs of the more efficient units.

Staffing a radiotherapeutic physics-department has become a universal problem owing to the demands of industry on the supply of skilled physicists. South Africa is somewhat better off in this respect than most other countries, since the industrial demands have not yet developed greatly. The successful construction and operation of the cyclotron, a far more complicated instrument than any radiotherapy generator, by a locally-trained staff in Pretoria, shows that this country does not lack physical skills. Because of the greater simplicity in beam-direction and dosimetry, supervoltage radiation actually requires less computational work on the part of the physics staff than the detailed isodose-planning necessary if conventional radiotherapy is to reach comparable efficiency.

It must be remembered that physicists are not required to operate and maintain the radiation generators; their function lies in the planning and execution of specific treatment-policies developed in consultation with the radiotherapist. With this end in view, 3 of the Provincial radiotherapy-centres have already appointed their physics staffs, and these departments will serve as nuclei for training hospital physicists in this country. When the time comes to install the new units, there will be no lack of skilled physicists in our hospitals, and indeed some Provincial centres have already made advanced plans for expansion, including the supervoltage units described.

#### ORGANIZATION OF A REGIONAL CENTRE

We have shown that the optimal treatment of cancer, taking advantage of modern developments in therapy, requires the development of large regional centres in which the expensive and complicated equipment can be housed, and the large clinical and ancillary staff can be concentrated. To meet the requirements of this country 6 regional centres are needed, but with its more widely dispersed communities it is necessary to compromise between the advantages of a highly centralized organization like the Holt Radium Institute in Manchester, and the difficulties in transporting country patients to centres in the large cities. One solution suited to the mixed urban, suburban and rural, multi-racial communities of South Africa, embodies a regional centre based on existing facilities and organized at 3 levels:

1. *The Central Unit*, housing the administrative head and his offices; the senior radiotherapists, physicists, engineers, radiographers, workshop technicians, clerks, radium custodian and librarian; the radium and isotope store; physics and biology laboratories; records and statistics files; teaching facilities; protection service; and major special equipment, including the 2 supervoltage units described above.

2. *Two Hospital Sub-centres*, European and non-European, each with conventional high-voltage and superficial therapy machines, wards, theatres, out-patient facilities, and departmental staffing for radical radiotherapy of potentially curable cases.

3. *Several Peripheral Clinics*, under the direct control of the sub-centre, strategically sited in populous suburban or rural areas, each having one inexpensive versatile medium-voltage therapy machine and one radiographer, with a radiotherapist sent from the centre for one or more weekly sessions to see new and follow-up cases and to prescribe treatment for those non-malignant conditions and simple palliative procedures which do not require the facilities and technical precision available at the larger hospitals.

Since many hospitals would be encompassed in a single regional scheme, it would be advisable for the Centre to be under direct Provincial control rather than under several hospital boards, although existing hospital radiotherapy facilities would have to be taken over.

That these proposals are workable is shown by the success of a similar organization in Australia, where the population distribution resembles ours. By an Act of the State Parliament of Victoria, a Cancer Institute has been established with a Central Unit at Melbourne and Radiotherapy Sub-centres at several surrounding hospitals. After exhaustive discussion among administrators, radiotherapists and physicists, somewhat along the line indicated here, the Institute has purchased from Metropolitan-Vickers, Ltd., a 4 MeV linear accelerator installed at a total cost of £65,000!

It is an interesting comparison to note that these developments in Australia were brought about through the activities of the 'Cancer Institute Board', a constitutional body whose general aims resemble those of our National Cancer Association but who, unlike our Association, have undertaken to develop all

the necessary facilities for the efficient treatment of cancer in a State institution, to establish centralized radiotherapy units, and to support research directed to these ends, before embarking upon cancer education drives, detection centres, and 'fundamental' research. The officers of our Association might do well to note this logical order of development in cancer services, and the necessarily close liaison between this Board and the State administration; they might perhaps consider emulating this example by establishing a similar liaison with our Provincial administrations and appointing Provincial-hospital radiotherapists, surgeons and pathologists to their committees.

#### SUMMARY AND CONCLUSIONS

The future of cancer therapy is South Africa lies with centralized regional institutions, each based on a population of 2-3 millions and treating up to 2,000 new cases a year.

About half of these cases would benefit materially from super-voltage radiation, most conveniently generated by telecurie

isotope units or linear accelerators, either or both being installed in each centre according to the turn-over of patients.

In such large centres the supervoltage units virtually pay for themselves on account of their larger output and simpler operating techniques, compared to the several conventional machines that would otherwise be needed to handle the same turn-over.

The National Cancer Association should work in close liaison with the Provincial hospital services and give active support to the provision of radiotherapy projects on the most modern lines. Such activity by the Association would be worthy of the generous public support it has received.

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### THE NATIONAL CANCER ASSOCIATION OF SOUTH AFRICA

The National Cancer Association of South Africa have issued the following information:

An amount of £325,091 10s. 8d. had been received by the Cancer Appeal Fund up to 31 December 1955. Promises outstanding amount to £54,789. At a recent meeting of the Council of Management of the National Cancer Association Dr. Lewis S. Robertson, President of the Association, spoke appreciatively of the voluntary efforts of Dr. van Eck and his Committee and the 381 Fund Raising Committees. The total expenses incurred in collecting money amounted only to £23,235 13s. 8d., or 7.1% of total receipts. Fund Raising Committees throughout the country were still active and collections were still proceeding, which it was hoped would ensure a regular annual income in order that the fight against cancer should continue unhampered.

The subscriptions in the Transvaal had amounted to £148,563 13s. 7d., in the Cape Province to £61,805 18s. 1d., in Natal to £40,947 12s. 9d. and in the O.F.S. to £15,013 4s. 6d. The South African Police and the South African Railways were responsible for the collection of £30,966 8s. 0d. and £27,254 4s. 8d. respectively. Additional collections since 1 January 1956 have not been included in these figures.

All sections of the public of South Africa are united in their desire to fight cancer, and the Association hopes to have the assistance of every man and woman in the country prepared to assist in stage two, which is now being organized. So far the emphasis has been on fund raising. Organised volunteers can now do much to assist the National Organization in educating the public. Committees which have hitherto existed solely for raising funds should seriously consider forming themselves into Committees to carry out the Association's objects in their areas. Natal has already taken steps to form a Branch Committee while

in the Cape efforts will shortly be made to form a Cape Western Branch of the Association.

The following are some of the steps already taken in 1956:

**Public Education.** Pamphlets have been distributed throughout the country and new pamphlets, notably one on breast cancer, are in the course of preparation and will be distributed as they become available. Five educational films for lay audiences are on order and it is hoped that a cinematograph unit will shortly be available for educational tours throughout the country. The question of an exhibition is receiving the attention of experts.

**Information from Doctors.** Replies received from the medical profession throughout South Africa to a questionnaire on the care of the cancer patient are in the process of being analysed. Most interesting and valuable information has been received, which should greatly assist in guiding the Association on the needs of cancer sufferers in regard to nursing services, hospitalization and other relevant matters. The Association urges doctors throughout the country who have not yet completed the questionnaire to do so without delay.

**Professional Education.** More than £3,000 has already been spent during 1956 on scientific overseas publications circularized to the medical profession. The publication of a quarterly professional bulletin is contemplated and details are now receiving attention. Approval has been given for the supply of scientific publications on cancer to Universities and Institutions training students to supplement their own existing libraries. Three films for professional education are already available and three more are on order from the United States of America.

**Research.** Fellowships and grants for research work on cancer to the value of £26,546 6s. 10d. have already been paid out, and it is hoped towards the end of the year to be able to publish progress reports on the various projects undertaken.

### THE RIGHT TO DISPENSE

The parliamentary session came to an end before the Medical, Dental and Pharmacy Amendment Bill had advanced beyond the first-reading stage. According to a press report, the Minister of Health, in announcing that this was going to happen, referred to the clause which had been deleted from the Bill before it was brought into Parliament and which would have had the effect of

destroying the right of most medical practitioners to dispense medicines for their own patients.

Mr. Naudé said that it was possible that the reinstatement of the clause might come before the House next session, and suggested that the delay of 6 months, which would now occur might be used for discussions between the professions interested in the clause.

### IN MEMORIAM

DR. EDWARD NEIL O'NEILL, M.R.C.S. (ENG.), L.R.C.P. (LOND.)

Dr. J. L. McLetchie, Director of Medical Services, Eastern Region, Nigeria, writes: Dr. Edward Neil O'Neill, who died on 16 May 1956 at the Rondebosch Hospital at the age of 64, was an artillery officer in the 1914-18 war and then studied medicine. After quali-

fying in 1928 he worked first with a mining company in Nigeria before joining the Colonial Medical Service in which he served for 20 years until his retirement. The latter part of his service was spent as principal of a school for training dispensary attendants

and field assistants. After retiring Dr. O'Neill lived for more than 12 years in Cape Town.

Dr. O'Neill was a man of great charm, known best to a small circle of close friends of whom I had the privilege to be one. He

found his metier in, and thoroughly enjoyed, the teaching of African Assistants. Many of those who passed through his school will mourn his death.

DR. J. M. COPLANS, L.R.C.P., L.R.C.S. (EDIN.), L.R.F.P.S. (GLASG.), L.D.S., R.C.S. (ENG.)

Joseph Moses Coplans, who died on 5 June 1956 at the age of 70 years, was born in Canterbury, Kent, on 3 April 1886. He was educated at the Simon Langton School, Canterbury, and qualified L.R.C.P., L.R.C.S. (Edin.), L.R.F.P.S. (Glasg.) in 1912.



Dr. J. M. Coplans

While a student at St. George's Hospital, London, he was employed as cartoonist to the London Jewish Chronicle and produced a series of political and current cartoons on Jewish national life. Many of these cartoons were reproduced in the Review of Reviews. He was the author of *Blood Libel*.

Dr. Coplans practised as a dental surgeon in Cape Town until 1916, when he joined the S.A.M.C., with which he served in France as a medical officer. During the battle of the Somme he was injured by high explosive and was returned to Britain, where he became Director of Dental Services to the King Albert War Hospitals. For his services to the Belgian army he was decorated with the Order of the Knight of the Crown of Belgium, an honour which was also accorded to his elder brother, Dr. Myer Coplans, O.B.E., D.S.O., M.D.

In 1921 he proceeded L.D.S., R.C.S., Eng. He returned to this country after the war to practice dental surgery in Johannesburg, and in 1924 he stood as Labour candidate for the constituency of Von Brandis. He was always concerned with the rights of ex-service men and was politically active in this direction. He later decided to return to general medicine and at the time of his death had been practising medicine in Cape Town for some years.

Dr. Coplans was of a highly inventive nature and his inventions covered fields other than those in which he worked. He invented and developed the giant reflecting ophthalmoscope, which was exhibited before the Royal Society in 1932. He was interested in stereoscopic cinema photography and developed a camera which produced startling stereoscopic effects. He devised an ingenious method of reproducing painting with full impasto effect. His article 'Notes of New Method and Apparatus for Ethylchloride Anaesthesia' appeared in the *British Medical Journal*.

His love of drawing remained with him always, and while practising as a dentist he produced a small carving in bronze which was carried out by means of dental drills. He began to model vigorously and produced a series of sculptured heads of famous men. A bust of the late Field Marshal J. C. Smuts is in the University hall of St. Andrews, a bust of the late Oom Paul Kruger stands in the Kruger Museum, Pretoria, and the bronze head of the late Tielman Roos is in the Supreme Court, Bloemfontein. The last head, a vigorous bust of George Bernard Shaw, was accepted by the National Gallery of Eire and stands next to those of Rodin and Troubetzkoy; replicas stand in the Fogg Museum, Harvard, and the British Museum.

Dr. Coplans is survived by his wife, two sons and a daughter.

## PASSING EVENTS : IN DIE VERBYGAAN

Dr. Noel H. Aldridge, M.B., Ch.B. (Cape Town), D.M.R.D. (R.C.P. & S.), formerly Instructor in Radiology at the John Hopkins Hospital Baltimore, USA; and Registrar in the Department of Radiology at the General Infirmary, Leeds, England, has been appointed Assistant Professor of Radiology at the Guthrie Clinic, Sayre, Pennsylvania, USA. He will assume duties there on 1 July 1956.

\* \* \*

South African Council for Scientific and Industrial Research: Post-Graduate Bursaries for Directed Research (Overseas). The C.S.I.R. invites applications for bursaries for work at approved overseas institutions. The value of the bursaries will be: for work in the United Kingdom, £500 per annum, for work on the Continent of Europe, £600 per annum, for work in the United States of America, £800 per annum. Application may also be made for a travel grant of not more than £220. Bursaries will be tenable from 1 October 1956 for one year at a time, and may be renewed if satisfactory progress reports are received.

Applicants must submit programmes of research, must undertake to return to the Union on completion of the bursaries, and

must make their own arrangements for entrance into approved overseas institutions. Forms and regulations are obtainable from the Registrars of the South African Universities, or from the Secretary-Treasurer, Council for Scientific and Industrial Research, P.O. Box 395, Pretoria. Applications should, where possible, be submitted in time to reach the Council not later than 30 June 1956.

The following are included in the fields of research which may be eligible for bursaries: Biophysics; Hospital physics; Chemical concentration methods of trace elements by modern techniques; Human nutrition, (a) the role of enzymes in human metabolism, (b) electron-microscopic studies of blood morphology in malnutrition and undernutrition, or (c) tissue culture with special reference to the study of the interaction of nutrients; Biochemistry of plant and animal metabolism; Physiometric methods (the study of measuring techniques in applied psychology, especially in relation to the construction of personnel selection tests, questionnaires and the collection of accident, absentee and labour-turnover statistics; Industrial sociology—a study of the sociological factors that influence productivity; Work study in relation to productivity; Microbiology of foods.

## REVIEWS OF BOOKS : BOEKRESENSIES

### PUBLIC HEALTH

*Modern Public Health for Medical Students.* By I. G. Davies, M.D., F.R.C.P., D.P.H. Pp. 487 with illustrations. 30s. London: Edward Arnold (Publishers) Ltd.

Contents: Chapter 1. The Nature and Scope of Public Health. 2. Heredity and the Public Health. 3. Nutrition and the Public Health. 4. The Measurement of Health. 5. Health and Welfare Legislation. The Organization of Medicine.

Social Care. 6. The National Health Service Acts, 1946-52. 7. National Insurance. 8. Diseases of Special Social Importance. 9. Mental Health. 10. Occupational Health. 11. Rehabilitation and Resettlement. 12. Handicapped Persons. 13. Maternal Health and Welfare. 14. The Health and Welfare of the Infant and Young Child. 15. The School Child. 16. Communicable Diseases. 17. International Health. 18. Accidents in the Home. 19. Health Education. Index.

This is a public-health text-book with a difference, in that the author has omitted technical descriptions of the sanitary aspects of water supply, drainage and general sanitation. He has concen-

trated more on the wider field of 'social pathology' and has attempted to show the significance and importance of the community aspects of ill-health and to teach the purpose of the legislative, administrative and social measures which the state has adopted for the maintenance of the public health. The diversity of the subjects can be seen from the chapter titles above and as it was written for students and practitioners in the United Kingdom it is inevitable that there should be extensive references to the progress made in a 'welfare state'. It is an interesting book and most informative.

A.H.T.

## OCCUPATIONAL THERAPY IN PSYCHOLOGICAL MEDICINE

*Textbook of Occupational Therapy. With Chief Reference to Psychological Medicine.* By Eamon N. M. O'Sullivan, B.A., M.B., D.P.M. Pp. 319—x with illustrations. 21s. 0d. London: H. K. Lewis & Co. Ltd. 1955.

*Contents:* 1. Introduction. 2. Definition and History of Occupational Therapy. 3. Principles, Rules, Objects, and Advantages of Occupational Therapy. 4. Classifications and Subdivisions of Occupational Therapy. 5. Development and Organisation—Administrative Personnel. 6. Development and Organisation (cont.). Sections and Units. Handicraft Section. 7. Sections and Units (cont.). Recreational Section—General Analysis. 8. Sections and Units (cont.). Recreational Therapy Section—Special Analysis. 9. Sections and Units (cont.). Re-Educational Section. 10. Sections and Units (cont.). Commercial Section. 11. Psychological Analysis—Mental Diseases. 12. Psychological Analysis (cont.).—Mental States. 13. Craft Analysis—General. 14. Special Craft Analysis—Willowcraft, Canecraft, etc. 15. Special Craft Analysis—Woodcraft. 16. Special Craft Analysis—Woodcraft (cont.). 17. Special Craft Analysis—Weaving. 18. Special Craft Analysis—Weaving (cont.). Bibliography. Index.

Dr. Sullivan has obviously waded through a great deal of scattered literature on the subject and been most painstaking in putting his material ship-shape in order to give the correct modern approach.

The development of occupational therapy throughout the world, and in particular at the Killarney Mental Hospital, is mentioned. He stipulates that occupational therapy is primarily a form of treatment which must at all times be under expert medical direction: that it must be evolved on a definite system and applied methodically; that the patient's competence and interests must be considered in relation to the work to be prescribed, the treatment being judged only by its effect on the patient; and that the occupational therapist must have the necessary technical knowledge, a special aptitude for imparting instructions, and a suitable temperament and manner.

The advantages of occupational therapy are discussed as: (1) psychological—the effect of work, the personal reactions of the patient and the benefits to the hospital and community; (2) physical—a properly planned programme of work and exercises, which must improve the bodily health and create favourable interactions between mental and bodily processes; (3) economic—its value to the hospital and the community.

The author discusses in detail the organization required to administer a large mental hospital. The various mental states and symptoms of patients referred for treatment are outlined. General craft-analysis is explained, while basketry, woodcraft and weaving are fully considered under the following headings: (1) Qualities, both subjective (sedative or stimulative) and objective—complexity, flexibility, novelty, variety and utility. (2) Economic—(a) equipment, (b) materials and (c) sales; emphasis being laid upon the fact that the therapeutic value must always be foremost. (3) Technical—covering the various operations and activities met with. (4) Psychological. (5) Physical. (6) Advantages. (7) Disadvantages.

This book fills a gap, and makes good reading. It has a large bibliography and an excellent index. And it is highly commended to the reader.

R.R.B.

## A SHORT TEXT-BOOK OF SURGERY

*A Short Text-book of Surgery.* Sixth Edition. By C. F. W. Illingworth, C.B.E., M.D., Ch.M., F.R.C.S. (Ed.), F.R.F.P.S. (Glas.), Hon. F.A.C.S. Pp. 628 + viii with illustrations. 37s. 6d. London: J. & A. Churchill Ltd. 1955.

*Contents:* 1. Safety Factors in Surgery. 2. Healing and Repair of Wounds. 3. Wound Infections. 4. Actinomycosis. 5. Tuberculosis. 6. The Venereal Diseases. 7. Shock and Haemorrhage. 8. Burns and Scalds. 9. The Skin and Subcutaneous Tissues. 10. The Muscles, Tendons, Tendon Sheaths and Bursae. 11. The Peripheral and Autonomic Nerves. 12. The Blood Vessels. 13. The Lymph Glands and Vessels. 14. Affections of Bones. 15. Affections of Joints. 16. The Shoulder Girdle and Arm. 17. The Elbow Region. 18. The Forearm, Wrist and Hand. 19. The Hip and Thigh. 20. The region of the Knee. 21. The Leg, Ankle and Foot. 22. The Skull and Brain. 23. The Spine and Spinal Cord. 24. The Eye, Ear, Nose and Throat. 25. The Face, Mouth, Tongue, Jaws. 26. The Neck. 27. The Thyroid and Parathyroid Glands. 28. The Larynx, Pharynx and Oesophagus. 29. The Breast. 30. The Thorax. 31. The Abdominal Wall and Hernia. 32. The Peritoneum. 33. Abdominal Emergencies. 34. The Stomach and Duodenum. 35. The Intestines. 36. The Rectum and Anus. 37. The Biliary Tract. 38. The Pancreas. 39. The Spleen. 40. The Adrenal Glands. 41. The Appendix. 42. The Kidney and Ureter. 43. The Bladder and Urethra. 44. The Male Genital Tract. 45. The Female Genital Tract. 46. Radiotherapy and Physiotherapy. Index.

This latest edition of this well-known short Textbook of Surgery will be well received by all who have used and admired its predecessors. That it is the 6th edition in sixteen years shows the demand for it, and is evidence of its popularity. It is probably the best solution available of the problem of constructing a comprehensive, but short, text-book of surgery.

In such a work it is impossible to please everybody's choice of what to include and what to omit, but Professor Illingworth, like Agag, has walked delicately and achieved a maximum result with a minimum economy of effort as expressed in the number of pages.

The illustrations are good, the printing and production pleasing, and the uniformity of style and approach make it very readable.

R.D.H.B.

## CORRESPONDENCE : BRIEWERUBRIEK

## MEDICAL SERVICES AND MEDICAL ETHICS

*To the Editor:* For some time past I have been perplexed by the frequent use in articles appearing in the *South African Medical Journal* of the words 'ethics', 'ethical' and 'unethical' in contexts which appear to deny to them their ordinary meaning, in current usage, of 'morals', 'moral' and 'immoral'; and when, recently, I found in the *Journal* of 12 May last a memorandum written by Dr. M. Shapiro and four other doctors entitled 'The Provision of Medical and Dental Services in relation to Medical Ethics' I hoped that I might gain some understanding of the sense in which these words are used by the Medical Association and its office-bearers.

Finding that, although the word 'ethical' appears 8 times in the memorandum, 'ethics' once and 'unethical' once, there is nowhere any definition of them either in express terms or by implication from the immediate context it occurred to me that a study of the memorandum's description of the various practices which it submits for reprobation might serve to lighten my darkness. For it is a legitimate inference from the title that these practices are condemned as being unethical.

Leaving on one side, at least for the time being, the authors'

excursus into the field of law and legal procedure, these practices are:

A. The *modus operandi* of certain medical aid and medical benefit societies;

B. The levying by Provincial hospitals of fees from patients for radiological and other services performed by full-time salaried medical officers; and

C. The granting by the South African Institute for Medical Research of discounts to nursing-home owners to cover costs of collection by the latter of charges payable to the former.

It is not easy to analyse the indictment presented against the medical aid and medical benefit societies. It is said of the Vanderbylpark Sick Benefit Fund that it reserves the right 'in defiance of medical professional opinion as represented by the Medical Association of South Africa' to extend its operations, at its own sole discretion, to include new members and groups of members. It is added that for these (and presumably for its older members) it provides medical services 'on the basis of a closed panel of full-time medical officers appointed by the Fund'. Is it perhaps the latter averment that assigns a breach of 'ethics'? Apparently not; for objection is not made to the original formation of the Fund, but only to its expansion *mero motu*. Is it then to be inferred that it is ethical for Tom, Dick, Brown and Jones to associate

together for the purpose of diffusing the impact of the high cost of medical services, but quite unethical that they should allow Harry and Robinson to join the party? Or does the obliquity of the acts result from their doing so without the consent, and even in defiance, of the South African Medical Association, which can convert the 'unethical' into the 'ethical' by a stroke of its august pen?

The indictment of the Mines Benefit Society appears to have similar grounds, though the method of remuneration of its general-practitioner medical officers is somewhat different.

The main charge against the Northern Medical Aid Society is also one of 'wilful and serious' expansion, facts being cited to show that it cannot set up the plea in extenuation of Marryatt's housemaid—that the fruit of its misdoing is only a little one. There is another count, viz. that it requires newcomers to its ranks to pay what is in effect an entrance fee calculated as the equivalent of the *per caput* share of the existing members in the net assets of the Society. The ground of objection here is not evident, for the Society is presumably an association not for profit and this, as well as other accruals, goes to swell the funds available for meeting the costs of medical service to the members, including the remuneration of doctors. Only in this latter respect does this exaction of contribution seem to differ from that ordinarily made by a firm of doctors from a would-be partner.

The paragraph closes with the following sentence: 'We regard this arrangement' (i.e. autonomous expansion) 'as a clear case of exploitation of the medical profession'. Here again assertion seems to be used as a substitute for demonstration (c.f. 'His aunt Jobiska said "everyone knows that a Poble is better without his toes"'). Only if the remuneration of the doctors employed by these societies is inadequate—and that is not averred—could there be said to be exploitation.

Turning now to the matter of Transvaal Provincial Administration and its levying from private patients in hospital of fees for radiological services, it appears that the arrangement was approved by the Medical Association provided that the amount collected was paid into a fund to be used to the advantage of the medical profession. It must be presumed then that the arrangement was regarded by the Association as 'ethical'. All that has since happened is that it has been found that it is impossible to alienate the money from the Provincial Exchequer and consequently it is being applied to the benefit of the residents of the Province generally. Is it to be held that the practice is unethical if the general public benefits but ethical if the proceeds are applied to the advantage of the medical profession and not only that of the doctors who have done the work? Does the character of the receiver sanctify the theft? I should perhaps add that I am disposed to agree with the authors that the present practice is unethical, but on different grounds. In my opinion, if the money so collected is not required, or may not be used, to defray the Administration's costs in providing the services, its collection is improper, though not, I think illegal.

Lastly there is the question of a discount to cover costs of collection of fees. Now it is admitted that there is nothing unethical in the employment, on a commission basis, of an agent to collect bad debts; and it seems to follow that the employment of an agent to collect debts before they become bad is also unobjectionable. Does the fact that the amount paid, whether by way of discount or of commission, is so large as to afford a substantial profit to the agent, affect the character of the transaction. If the agent, being the owner of the nursing-home, as in the case under discussion, has the selection of pathologists in his hands, there is a marked inducement to him to prefer this generous principle to its competitors, and that may well be regarded as, at the least, undesirable though hardly immoral. But does the owner of the nursing-home have the power of selection? My impression is that it rests with the patient's medical attendant. But again I find myself in agreement with the authors, and again on different grounds. If the Institute can, as it would seem that it can, afford economically the needed service at 85% or less of the fee charged to the patient, the latter is grossly overcharged. To my mind that is improper to the verge of being unethical.

A few words on the questions of law and legal procedure raised in the memorandum. It seems quite unnecessary to cite a judgment of the District Court of Iowa U.S.A. in and for Polk County (a tribunal believed to have much the same standing and jurisdiction as a Magistrate's Court of the Union) on the effect of a statute of that State and to assume, without knowing, or at least without disclosing, the wording of that statute, that it corresponds

with that of the Union statute dealing with the same question. The only question is, 'What is the Union statutory provision and what does it mean?' The answer to the first part of this question is to be found in Section 24 (1) of the Medical, Dental and Pharmacy Act 1928 ('No person shall be entitled to practise within the Union as a medical practitioner . . . unless and until he has obtained a registration certificate signed by the registrar') and in Section 34 (1) of that Act ('Any person not registered as a medical practitioner who—(a) for gain, practises as a medical practitioner . . . shall be guilty of an offence . . .'). Can a person who or which habitually employs qualified practitioners to perform acts specially pertaining to their calling as such be held to 'practise as a medical practitioner'? If it be so held then not only medical aid and benefit societies are practising, and practising illegally, for they cannot be registered, but so are the Mines, most Municipalities, and a whole host of other employers including the Government and in particular the Railway Administration. It is an established rule of interpretation of statutes that regard may, and should, be had to the consequences of the adoption of a particular interpretation, and it seems quite improbable that the wide meaning of 'practise' which the authors of the memorandum seem to favour could ever be authoritatively approved. Even in this unlikely event the practising, though illegal, would be punishable only if done 'for gain' and the provisions of Section 34 would consequently not apply to bodies such as medical aid and medical benefit societies which, in all known cases, are bodies formed 'not for profit'.

In the memorandum it is asserted that 'it can be readily appreciated that the entire process of law would be subverted if corporations and companies were to be granted the right to nominate and remunerate the lawyers who could be chosen to defend in the Courts of Law the individual interest of all persons who fall under the control of such companies—whether by compulsion or voluntary submission'. This again is an attempt to support a doubtful proposition by reliance on one even less arguable, for this is precisely what is now being done by various corporations (e.g. insurance companies, certain trade unions and the Automobile Association) and, so far as has appeared, without the dire consequences apprehended in the memorandum. One may even venture to suggest that the formation of 'legal benefit societies' on the lines of medical benefit societies would not impair the administration of justice but would give to persons of moderate income the access to superior courts which is now denied by the high cost of litigation to all but the wealthy.

And so the examination results in a *reductio ad absurdum*, for the only conclusion which it suggests is that in the view of the Medical Association a practice or course of dealing is 'ethical' or 'unethical' as it conduces to or is in conflict with the financial advantage of the medical profession. And that is, of course, quite unacceptable.

S. Maynard Page

Mines Benefit Society  
P.O. Box 8603  
Johannesburg  
28 May 1956

1. Shapiro, M., Struthers, J. H., Turton, E. W. du Toit, J. G. and Gluckman J (1956): *The Provision of Medical and Dental Services in Relation to Medical Ethics*, S. Afr. Med. J., 30, 458.

#### A REPLY BY DR. SHAPIRO

To the Editor: Since Mr. Maynard Page is such a keen student of our *Journal*, we should have expected that he would have learnt by now that the term 'medical ethics', to which he appears to be semantically allergic, means merely that standard of professional conduct expected of a doctor by his own colleagues—not as it may be adjudged by the public or by legal authority. Thus, what Mr. Page may consider to be an acceptable business arrangement might, in the case of a doctor, be regarded by his colleagues as 'dichotomy', than which there are few greater offences in the profession's code of honour.

Mr Page's disparaging reference to the District Court of Iowa as 'a tribunal believed to have much the same status and jurisdiction as a Magistrate's Court of the Union' comes strangely from one who occupied a worthy and distinguished place in just such a Court in his own country. Assuming that his belief with regard

to the status of this Court is correct (he himself is not sure on the point), how does this detract from the wisdom, justice or validity of its findings? Even our own magisterial courts have had their exponents of forensic brilliance. As a lawyer, Mr. Page would have been well advised to have studied this penetrating judgment before presuming to criticize it. He may be encouraged to learn that eminent Senior Counsel considers it to be equally valid in terms of South African statutory law.

M. Shapiro

Sasbank Buildings  
66 Market Street  
Johannesburg  
8 June 1956

#### WHAT ENDOCRINOLOGY IS NOT

*To the Editor:* A postprandial perusal of your editorial<sup>1</sup> of 26 May 1956 with the above-mentioned title, has stung me into waddling into print and there to cross swords with you concerning your blandly confident statement that 'fat comes from food and from nothing else'. Now I am a very fat person myself and I cannot, without protest, allow my adiposity to be dismissed with such an airy wave of the pen. I fear, sir, that you are in error for there is much more to fat than just food.

My own observations—and it should be borne in mind that I have a vested interest in the matter—of the contours and glossy billowing of the obese lead me to believe that fatness is nothing more or less than an Act of God. One is born that way or, at any rate, with a predisposition to obesity, which will with great certainty snake in on one round about the age of 30. I personally became well padded in almost imperceptible layers, or one may say annular rings, at the age of 28. Twenty years later I reached equilibrium and my weight became static at about 30 lb over the two hundred.

You have my word for it that fat is not an undivided blessing. Nevertheless it has important compensations, one being that it gives validity to smoking. On the other hand one cannot buy a suit 'off the peg' and the tailor requires an extra three-quarter yard; nor can one ever pretend to be someone else, a useful dodge reserved for the cunning thin linear types. Also, it gets insurance companies all hot and bothered and on a medical check-up one is reminded of miles and miles of superfluous capillaries and duly warned of the likelihood of an early demise. There is, it seems, no encouragement for the fat man anywhere except sometimes from his wife through a trick of accommodation that must be love. I have also time and again exploded the fallacy that an aldermanic paunch improves one's credit, maybe because I have no rolled-gold watch chain slung across mine.

With and without the well meant advice of deeply shocked cadaveric colleagues, I have on at least three occasions earnestly tried to do something about it. Rigorous dieting in one such hellish period made me drop 30 lb. On resuming my usual diet it was not long before I picked up a slick 45 lb. After that, simple arithmetic told me that dieting does not pay.

I do not subscribe to the hypothesis that a doctor must necessarily have suffered from a particular disease before he can treat it satisfactorily for, if that were so, our best specialists would be found in homes for incurables. I do say, however, let the fat doctors legislate for themselves, a privilege which the lean ones are not slow to take.

I feel that heredity must be held responsible for a lot of the fatness in this world. A liking for, say, cream cakes can fairly be classed as a contributory factor of minimal importance. If we can rightly speak of the rheumatic diathesis why cannot we with equal justification speak of the fat diathesis. The ingenious theory that obesity is a neurosis I take with a pinch of salt. Obesity has always been symbolic of the contented mind and of the stately measured tread. The ancients, if we are to believe such old people, mistrusted the 'lean and hungry look' at first sight, and the ancients have Shakespeare (or Bacon) on their side. The general belief that fat people are preoccupied with food is a misconception. They have no time for toying with imaginary bills of fare but get stuck right in like the realists they are. If it is difficult for a fat person to get thin it is equally difficult, indeed mostly impossible, for a thin person to get fat. So in this important aspect of the matter we have stalemate. We fat men have been comic figures for too long and that when we know well that many of the most accomplished gluttons are to be found in the ranks of

the thin. Our critics forget that though we cannot see our feet we rarely stumble or fall, showing that there is no imbalance anywhere.

To sum up, I am at one with the dictum that 'Nature abhors a straight line'.

Ernest Meiring

Kirkwood

9 June 1956

1. Editorial (1956): S. Afr. Med. J., 30, 487.

#### TOO MUCH 'PYGMALION' INTERFERENCE

*To the Editor:* One of those 'Full-Timers'<sup>1</sup> writes as follows in the *Journal* of 9 June: 'I must agree with some of our staunchest and most experienced members that the best service our pseudo-lawyers and pseudo-trade-unionists can possibly render to the Association is to retire from medical politics'. The majority of the profession feel the same way about this new trend in the Association affairs. Why have these staunch and experienced members handed over the reins to this junta and forsaken their responsibilities? Is it apathy or are they sick and tired of medical politics?

Why does the term expulsion from the Association figure so frequently in memoranda and debates. I envisage mass resignations and not expulsions unless there is a change for the better in the affairs of the Medical Association.

Member of the Association

13 June 1956

1. One of those 'Full-Timers' (1956): S. Afr. Med. J., 30, 552.

#### CHLORDANE POISONING

*To the Editor:* In reference to your editorial on this subject in the *Journal* of 25 February 1956<sup>1</sup> we should like to draw attention to the fact that, according to the South African Bureau of Standards, both Chlordane and DDT have the same acute toxicity values. Although it is correct that Chlordane is about 4 times more toxic than DDT to mammals when applied to the skin, Chlordane is only used in a 2% concentration as compared to DDT, which is today usually used in a 10% solution. The effective dermal toxicity of Chlordane is thus actually less than that of DDT and the effective acute toxicity only 1/5th that of DDT.

The following tables were supplied by the South African Bureau of Standards:

##### (a) Acute toxicity

Chlordane: LD 50 (oral) 225-250 mg./kg.  
DDT: LD 50 (oral) 250 mg./kg.

##### (b) Chronic toxicity: Both Chlordane and DDT have a comparatively low chronic toxicity.

##### (c) Dermal toxicity

Chlordane: 20% technical Chlordane in dimethyl phthalate—LD 50 of 780 mg./kg.  
DDT: 30% technical DDT in dimethyl phthalate—LD 50 of 2,800 mg./kg.

Furthermore, we wish to point out that whilst Chlordane was at one time prohibited in the United States for use in a space insecticide spray against common household insects and could only be applied for spot control with localized application, this restriction was removed last year and today Chlordane insecticide may be used in space-type domestic insecticides throughout America.

We should like to mention that extensive caution statements about inhalation, washing, etc. are printed on every label containing Chlordane and, indeed, any other insecticide which is sold, all insecticides having to be passed by the Registrar of Agricultural Remedies before being permitted to be sold in this country.

R. D. Hayden  
Director

P.O. Box 3389  
Johannesburg  
7 June 1956

General Chemical Corporation Limited

1. Editorial (1956): S. Afr. Med. J., 30, 181.